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Sulfate Radical Anion ($SO_4^{\bullet-}$) Mediated C(sp^3)−H Nitrogenation/Oxygenation in *N*-Aryl Benzylic Amines Expanded the Scope for the Synthesis of Benzamidine/Oxazine Heterocycles

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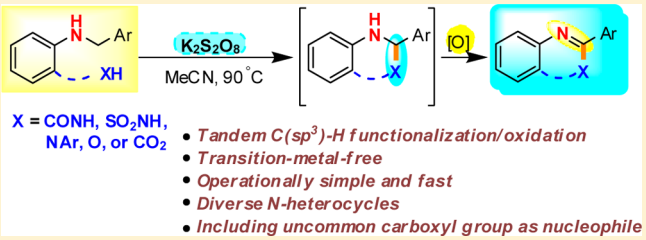
Supporting Information

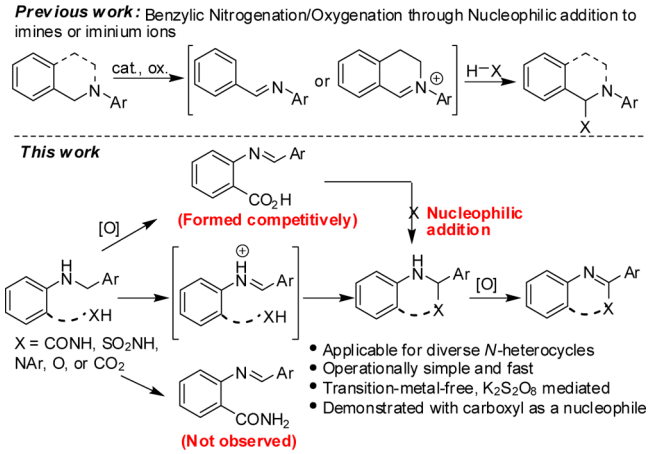
ABSTRACT: A transition-metal-free, $K_2S_2O_8$-mediated intramolecular oxidative nitrogenation/oxygenation of C(sp^3)−H in *N*-aryl benzylic amines followed by oxidation at the benzylic center has been developed for the synthesis of benzamidine/benzoxazine heterocycles, providing an expedient access to quinazolin-4(3*H*)-ones, *N*-aryl-2-arylbenzimidazoles, and 4*H*-3,1-benzoxazin-4-ones. A considerable amount of work dealing with the mechanistic study to understand the crucial intramolecular cyclization step largely favors an iminium ion as the key intermediate.



INTRODUCTION

The nitrogenation/oxygenation of benzylic C(sp^3)−H has long proven didactic value in organic transformation adding nitrogen-/oxygen-containing functionality to the benzylic position.[1] The α-functionalized benzylic amine is a central component of a wide range of compounds including pharmaceuticals, agrochemicals, performance materials, and bioactive natural products.[2] The capacity of benzylic C−H nitrogenation/oxygenation in benzylic amines to engender a unique structural feature with geminal carbon-hetero functionalities (*N*,*N*-acetal or *N*,*O*-acetal) at the benzylic position has motivated synthetic chemists toward the invention of a new, cost-effective, and environmentally benign approach. Further oxidation at the benzylic center could provide benzamidine/oxazine structural motifs that are ubiquitously found in many natural products, pharmaceuticals, and materials.[3] Historically, nucleophilic additions to the aryl imines using a variety of nitrogen and oxygen nucleophiles have rendered a circumlocutory approach to the nitrogenation/oxygenation of the benzylic C−H in *N*-aryl benzylic amines.[4] The oxidative benzylic C−H functionalization in benzylic amines, pioneered independently by Murahasi[5] and Li,[6] was largely explored on *N*-aryl tetrahydroisoquinolines and *tert*-*N*-alkyl anilines, generally in the presence of a transition-metal catalyst and sacrificial oxidant (Scheme 1).[7] Remarkably, a redox-neutral intramolecular cyclization,[8a,c] discernible from an intramolecular oxidative approach,[8b] has also been reported yielding various substituted fused *N*-aryl tetrahydroisoquinolines. A seminal contribution by Klussmann et al. has enabled in-depth understanding of the mechanism of these oxidative functionalizations, which relies on nucleophilic addition to the resulting aryl iminium species.[9] Conspicuously, an α-amino peroxide derivative was proposed to be an intermediate in the benzylic

Scheme 1. Benzylic C−H Nitrogenation/Oxygenation in *N*-Aryl Benzylic Amines



functionalization of *N*-phenyl tetrahydroisoquinoline employing CuBr/TBHP as oxidant. However, the oxidative benzylic C−H nitrogenation/oxygenation in *N*-aryl *sec*-benzylic amines (an acyclic benzylic amine), often effected in the presence of transition-metal catalyst/oxidant, has been the subject of a few reports.[10−12] The intramolecular cyclization of imines, formed in situ under oxidation conditions, paved the way for the synthesis of quinazolin-4-ones,[10] benzimidazoles,[11] and related nitrogen heterocycles.[12] Nonetheless, nucleophilic addition to the aryl imine or iminium species is the only dependable

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mechanism currently available in the literature for the functionalization of benzylic position in *N*-aryl benzylic amines.

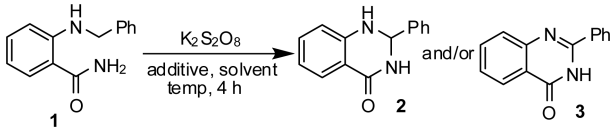
Despite these significant advances, the important questions still remain are, whether: (a) a transition-metal-free as opposed to transition-metal-catalyzed oxidative approach could be developed; (b) a single, nontoxic, inorganic oxidant that is compatible with environmental safety could execute a desired transformation; (c) a wide scope of nitrogen and oxygen nucleophiles including previously unexplored nucleophiles such as carboxyl group could be employed; and (d) a radical oxidative coupling mechanism distinct from nucleophilic addition to aryl imine or iminium species could be operative, in case a single oxidant is used. Therefore, development of a transition-metal free, nontoxic oxidant-mediated nitrogenation/oxygenation of benzylic C−H in *N*-aryl benzylic amines and subsequent oxidation to the nitrogen heterocycles containing amidine/oxazine structural motifs is of paramount importance. Nevertheless, an objective considering these questions collectively would be a formidable challenge.

Earlier, we demonstrated oxidative removal of benzylic methylene group and subsequent C−N bond formation in *N*-aryl benzylamine embedded in dibenzodiazepines utilizing a cheap, environmentally friendly powerful oxidant $K_2S_2O_8$.[13] Based on our previous experiences on the synthesis of nitrogen heterocycles,[14] we envisaged that intramolecular oxidative nitrogenation/oxygenation in *N*-aryl benzylamines, having an internal nucleophile substituted at the *ortho*-position in aniline ring, might be brought to fruition under transition-metal-free condition. Herein we describe, conceptually distinct from our previous report,[15] a transition-metal-free, single oxidant-mediated novel intramolecular oxidative benzylic C(sp^3)−H nitrogenation/oxygenation and subsequent oxidation, affording annulated nitrogen heterocycles under green conditions. The protocol appears to be generally applicable in the synthesis of nitrogen heterocycles including quinazolin-4-ones, benzimidazoles, benoxazoles, and benoxazin-4-ones, warranting wide applications of this protocol. The mechanistic study reveals that an iminium ion could be the key intermediate in the crucial intramolecular cyclization step. Furthermore, a rarely used nucleophile, for example, a carboxyl group, was demonstrated to participate with the iminium ion cyclizations affording benoxazin-4-ones.

RESULTS AND DISCUSSION

Our study commenced with the oxidative cyclization of readily available *N*-benzyl-2-aminobenzamide (**1**) to the corresponding dihydroquinazolinone **2** and its subsequent oxidized product **3**. $K_2S_2O_8$ was a judicious choice, largely derived from our previous study, as the primary oxidant for our optimization study.[13] $K_2S_2O_8$ was practically ineffective below 50 °C (Table 1, entry 1). A significant reaction was observed at 70 °C in 1 h affording **3** and dihydroquinazolinone **2** in 40% and 15% isolated yields, respectively (entry 2). A complete conversion of starting material was observed at 90 °C in 3 h yielding compound **3** in 80% yield (entry 3). However, lower stoichiometry (1 equiv) of $K_2S_2O_8$ reduces the yield (entry 4). Likewise, compound **1** gave a lower yield (55%) of **3** at higher concentration (entry 5). Other solvents produced inferior results (entry 6−8). While many other oxidants used in our study were ineffective, DDQ produced **3** in 50% yield (entry 9). The oxidative transformation was ineffective in the presence of a base (entry 10). The oxidation of **1** in the presence of allyl acetate, a well-known radical trap for $SO_4^{\bullet-}$,[16] gave only a trace amount of **3** (entry 11). The oxidation comes to a halt in the presence of a free radical quencher such as, TEMPO or ascorbic acid, suggesting that the reaction follows a radical pathway (entry 12). A comparable yield was obtained when the oxidation was carried out in the presence of 20 mol % AgOAc (entry 3 vs 13).[17]

Table 1. Optimization Study for the Synthesis of 3[a]



entry	additive	solvent	temp (°C)	3 (%)[b]
1		MeCN	RT-50	<10
2[c]		MeCN	70	40
3		MeCN	90	**80**
4[d]		MeCN	90	45
5[e]		MeCN	90	55
6		DCE	90	40
7		MeOH	90	15
8		Water	90	trace
9[f]		MeCN	90	50
10[g]	base	MeCN	90	0
11[h]	allyl acetate	MeCN	90	trace
12[i]	ascorbic acid or TEMPO	MeCN	90	0
13	20 mol % AgOAc	MeCN	90	79

[a]**1** (0.5 mmol), $K_2S_2O_8$ (1.0 mmol), solvent (5 mL), additive, if any (0.1−1.0 mmol), temp, 4 h. [b]Isolated yield. [c]Reaction was carried out for 1 h. [d]$K_2S_2O_8$ (0.5 mmol). [e]MeCN (2.5 mL). [f]Other oxidants such as TEMPO, $PhI(OAc)_2$, oxone, $(NH_4)_2S_2O_8$, or DTHP. [g]Base such as NaOH or K_2CO_3 (2 equiv). [h]Allyl acetate (2.0 mmol). [i]Free radical quencher (1.0 mmol).

The scope of intramolecular oxidative C(sp^3)−N coupling was manifested in the synthesis of quinazolinones[18] and their sulfonyl analogues from the readily accessible substrates **4**−**16** (Scheme 2). Despite sulfonamide pharmacophores inhabited in many drugs display a structural diversity, the general paucity of structurally related sulfonamide derivatives of quinazolinones relies on poor accessibility to these scaffolds. The substrates **4**−**16** were prepared by reacting 2-aminobenzamides or benzenesulfonamides with benzyl bromides in the presence of *tetra*-butylammonium bromide (TBAB) at 90 °C for 6 h. Under the optimized condition, *N*-benzyl-2-aminobenzamide **4** participated in the reaction yielding benzosultam **17** in 80% yield. The substrates **5**−**11** containing an electron-donating or -withdrawing group on the benzyl ring work eventfully affording various substituted quinazolinones or sulfonyl analogues **18**−**24** in good to excellent yields. However, the substrates **12**−**15** when exposed to the optimized condition for a longer period of time yielded the corresponding *N*-oxides **25**−**28** due to rapid oxidation of the corresponding cyclized benzosultams. Intriguingly, *N*-aryl *tert*-benzylamine **16** gave the oxidative cyclized product **29** in excellent yield (95%) under the optimized conditions. It is worthy to note that various functional groups were tolerated under the optimized condition, which could enable further synthetic manipulations.

The expanded scope of the current protocol was further demonstrated in the synthesis of benzimidazoles (Scheme 3).[19] The starting substrates **30**−**38** were prepared from 2-bromoanilines by base-mediated *N*-benzylation followed by palladium-catalyzed N′-arylation. Under the optimized condition, substrates **30**−**38** participated in the intramolecular

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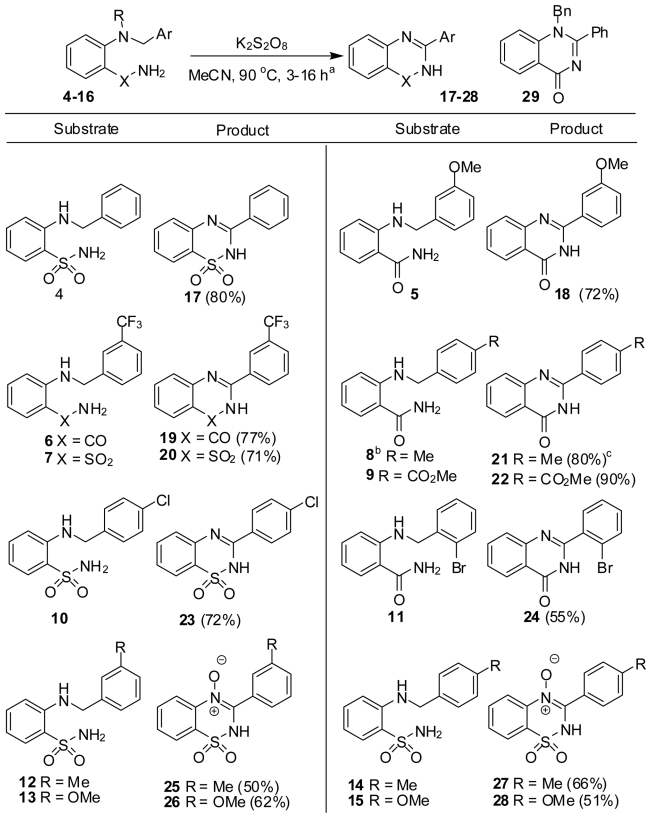
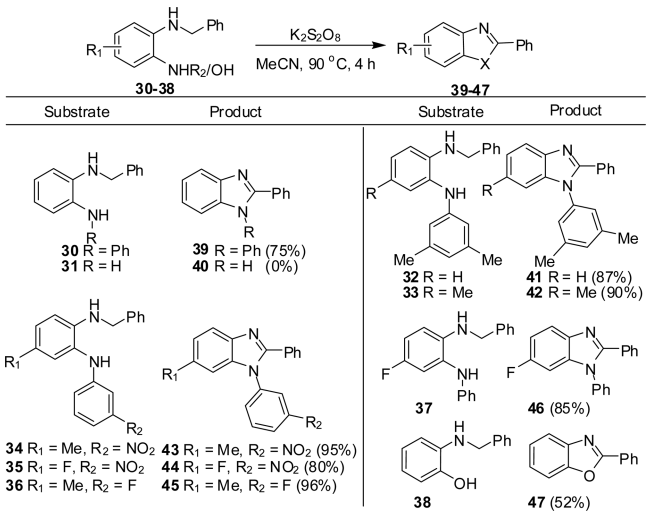
Scheme 2. Synthesis of Various Substituted Quinazolinones and Sulfonyl Analogs



[a]Time: 3−4 h for *N*-benzyl benzamides and 12−16 h for *N*-benzyl benzenesulfonamides. [b]Formed in situ from the reaction of 2-aminobenzamide and 4-methyl benzyl bromide. [c]Corresponds to the overall yield in two-steps (see one-pot synthesis)

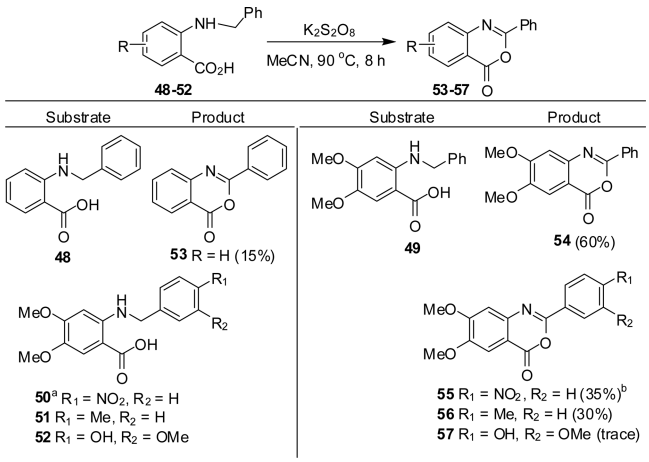
Scheme 3. Synthesis of Various Substituted Benzimidazoles and Benzoxazole



oxidative C−N/C−O bond formation, which upon further oxidation gave various substituted *N*-aryl-2-arylbenzimidazoles **39**−**47**. However, attempted preparation of benzimidazole **40** containing a free N−H was unsuccessful. To our delight, *N*-benzyl-2-aminophenol **38** undergoes intramolecular oxidative C−O coupling to form 2-aryl benzoxazole **47** in 52% yield.

Because of poor nucleophilicity of an aryl carboxyl group, a nucleophilic addition to aryl amines has been less successful to the synthesis of benzoxazin-4-ones, although they have been prepared in multisteps.[20] A direct access to benzoxazin-4-ones from *N*-aryl benzylic amines is, to the best of our knowledge, unprecedented. The starting substrates **48**−**52** were prepared from their corresponding 2-aminobenzoic acids and aryl aldehydes using reductive amination protocol, and the crude substrates were used in the next cyclization step without purification. Notably, the crude substrates were sufficiently pure except compound **50**, and their characterization data were found satisfactory. Thus, *N*-benzyl-2-aminobenzoic acid **48** gave benzoxazin-4-one **53** albeit in poor yield (15%) under oxidative condition (Scheme 4). A brief survey of different

Scheme 4. Synthesis of Substituted Benzoxazin-4-ones



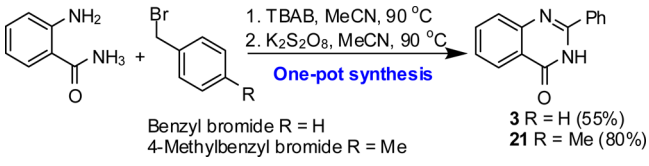
[a]Used the crude product obtained from the reaction of the corresponding benzoic acid and 4-methyl benzyl bromide. [b]Corresponds to the overall yield in two-steps.

substituents on two rings reveals their substantial influence in the product formation. The presence of two strong electron-donating groups in benzoic acid ring improves the yield by about 4-fold. However, the electron-donating or -withdrawing groups in benzyl ring have subordinate effect as observed in the synthesis of **55**−**57**. Noticeably, aryl aldehydes and 2-aminobenzoic acids were the two major byproducts in these reactions.

A one-pot synthesis of benzamidine heterocycles, exemplified in the synthesis of quinazolinones **3** and **21** from their corresponding commercially available materials, was achieved by reacting 2-aminobenzamides and benzyl bromides in the presence of TBAB followed by treating the reaction mixture with $K_2S_2O_8$ under the optimized condition (Scheme 5).

The following mechanism involving a key intramolecular cyclization of iminium ion is proposed in Scheme 6. Initially, reaction of **1** and sulfate radical anion ($SO_4^{\bullet-}$), generated in situ from $K_2S_2O_8$ under thermolysis,[21] could form a benzyl

Scheme 5. One-Pot Synthesis of Quinazolinones



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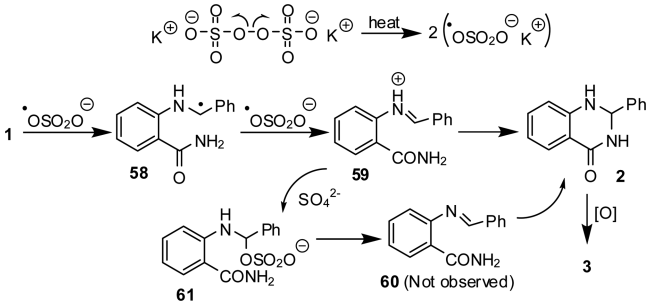
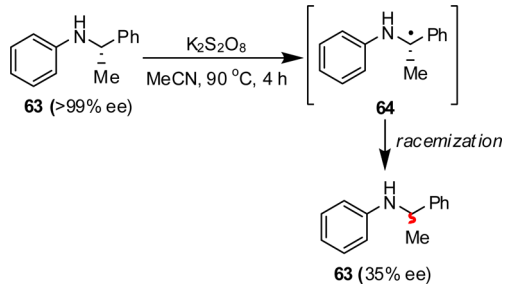
Scheme 6. Proposed Mechanism for the Benzylic C–H Functionalization



radical **58**, which upon subsequent oxidation could generate an iminium ion **59**. However, other pathways to form iminuim ion **59** are not ruled out.[7] An intramolecular nucleophilic addition in **59**, similar to that reported in literature,[7] followed by oxidation could give quinazolinone **3**. In a competitive manner, the iminium ion **59** could also produce *α*-amino benzyl sulfate **61** upon capture of a sulfate anion (SO_4^{2-}). Benzyl sulfate **61** could also give quinazolinone **3** via imine (**60**) formation followed by intramolecular nucleophilic addition and subsequent oxidation. Other pathways that could possibly form imine **60** are not ruled out.

Additional experiments were carried out to gain confidence on the proposed mechanism. The reaction of **1** under the optimized conditions in the presence of excess allyl acetate[17] gave only a trace of **3**, suggesting the direct participation of $SO_4^{\bullet-}$ in these oxidative transformations, disparate to Ag-catalyzed persulfate oxidation.[18] Under the standard conditions, an optically pure *N*-benzylaniline **63** resulted in a nearly quantitative recovery of starting **63** with extremely low optical purity (Scheme 7). The formation of a benzyl radical[22,23] **64**

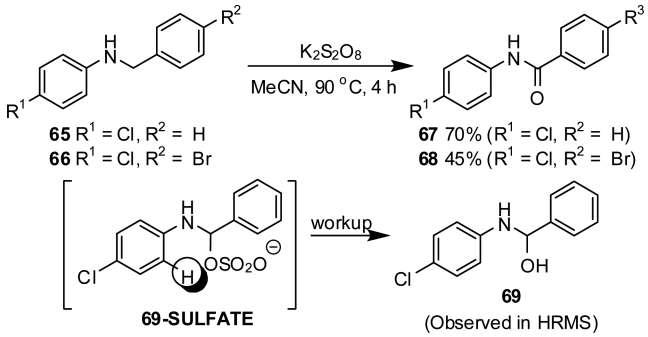
Scheme 7. Evidence for the Formation of Benzyl Radical



could cause racemization at the benzylic center. The presence of a considerable amount of unreacted starting **63** in the recovered sample could account for the low optical purity.

Evidently, a benzyl sulfate might be formed in the following experiments (Scheme 8). Under the standard conditions, reactions of *N*-benzylanilines **65**–**66** without having an *ortho*-functional group gave oxidized product *N*-benzoylanilines **67**–**68**. While attempted isolation of the benzyl sulfate (**69-SULFATE**) in the conversion of **65** to **67** was unsuccessful, a hydrolyzed product **69** was evident from the HRMS data (see the Supporting Information). In the absence of any internal nucleophile, the benzyl sulfates, if formed, could give imine or undergo further oxidation to *N*-benzoylanilines **67**–**68**. Hydrolysis of imines could generate the corresponding

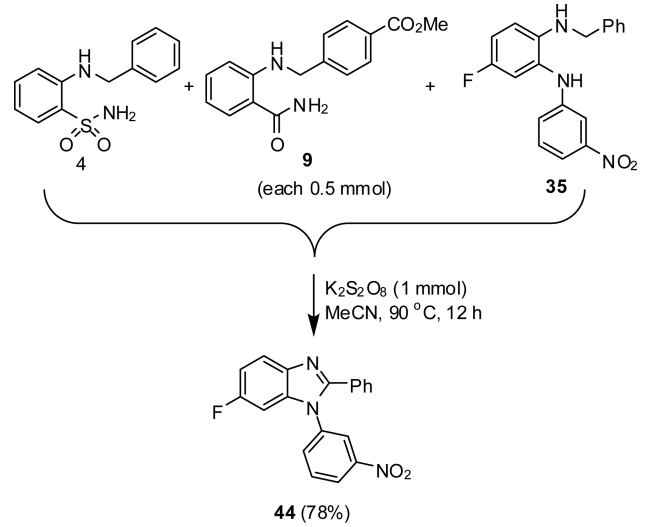
Scheme 8. Evidence for the Formation of Benzyl Sulfate



aldehydes that could account for nonpolar products formed in these reactions.

Notably, compounds **4**, **9**, and **35** appeared to be the most reactive substrates giving highest yields of the cyclized products in the respective series. However, a competitive experiment involving heating a mixture of **4**, **9**, and **35** (each 0.5 mmol) in the presence of $K_2S_2O_8$ (1.0 mmol) in MeCN (5 mL) at 90 °C for 12 h gave 2-arylbenzimidazole **44** as major isolable product in 78% yield, comparable to that obtained when **35** was reacted independently (Scheme 9). This experiment reveals that

Scheme 9. Competition Experiment



compound **35** has the superior reactivity among the three compounds. Probably, the enhanced nucleophilicity of nitrogen in NHAr group could facilitate intramolecular nucleophilic addition to iminium ion in **35**.

To understand whether imine **60** was formed in the reaction, a time course of the reaction at 70 °C (30 min, 1, 2, and 4 h) was followed by TLC, GC-MS, and ^{1}H NMR data. At any time point, the data collected did not indicate the formation of aryl imine **60** (see the overlapping ^{1}H NMR spectra of the reaction mixture at a time point with **2** and **60**, prepared independently). Furthermore, a more closer time point (every 5 min) in the 30 min to 1 h time block revealed the formation of unreacted starting material **1**, compound **2**, and quinazolinone **3** with a variable composition. Central to the mechanistic study was the finding that the formation of aryl imine **60** was not observed in the conversion of **1** to quinazolinone **3**. In stark contrast, aryl imine **62** and 4,5-

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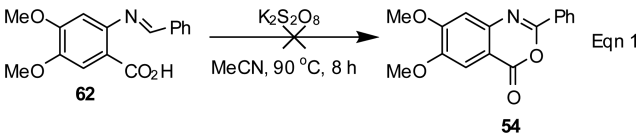
dimethoxyanthranilic acid were the two byproducts formed in the conversion of acid **49** to benoxazapin-4-one **54** (Scheme 4). More importantly, attempted conversion of **62** to **54** under the standard conditions was unsuccessful (eq 1). Therefore, formation of an iminum ion is likely involved in the reaction of **49**, which upon subsequent intramolecular cyclization could give **54**.



Collectively, these experiments are intuitive for the $SO_4^{\bullet-}$-mediated oxidative benzylic C–H functionalization that favors the intramolecular cyclization via an iminium ion as the key intermediate. The intramolecular cyclization in iminium ion **59** could give **2**, which upon further oxidation by $SO_4^{\bullet-}$ forms quinazolinone **3**. While *tert*-benzylamine **16** gave **29** under the optimized conditions, the reaction of **16** (0.5 mmol) and $K_2S_2O_8$ (1 mmol) in MeCN/MeOH (4 mL, 3:1) at 90 °C for 4 h gave **29** and **3** in 34% and 27% yields, respectively. The intramolecular nucleophilic addition of iminium ion **70** could give **29**. The formation of compound **3** in this reaction could be explained by the external nucleophilic attack of methanol. Thus, methanol could react with **70** to ultimately give **3** through a sequence of reactions as shown in Scheme 10.

In conclusion, an intramolecular oxidative nitrogenation/oxygenation of benzylic C(sp^3)–H bond, a widely sought yet elusive transformation, has been demonstrated in the synthesis of diverse benzamidine/benzoxazine heterocycles. The protocol described herein proceeds through a key step, intramolecular nucleophilic addition to imines followed by oxidation at the benzylic center. While the intermediacy of an imine **60** was not observed, aryl imine **62** formed in the reaction. Furthermore, a carboxyl group, rarely used as nucleophile in related iminium ion cyclizations, was used affording benoxazin-4-ones. While our protocol augurs interesting synthetic applications, developing an intermolecular version and subsequent applications to the synthesis of an antipsychotic drug Clozapine and understanding a detailed mechanism are the subjects of further investigation.

EXPERIMENTAL SECTION

General Methods. Unless noted otherwise, all reagents and solvents were purchased from commercial sources and used as received. All reactions were carried out using a clean oven-dried screw-capped reaction tube of 10 mL capacity. The progress of the reaction was monitored by thin-layer chromatography (TLC), wherein visualization was carried out with UV light (254 nm) and/or I_2 vapors. Column chromatography was performed on silica gel [100–200 mesh]. ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ or DMSO-d_6 as solvent using a 400 MHz spectrometer with Me_4Si as an internal standard. Coupling constants (J values) are reported in Hz. High-resolution mass spectra (HRMS) were obtained using electron spray ionization technique (ESI) and as TOF mass analyzer. All melting points were recorded using a melting point apparatus equipped with a calibrated thermometer and are uncorrected. Compounds **1**,[24] **2**,[25] **3**,[24] **17**,[18a] **30**,[13] **39**,[26] **47**,[11] and **63**[27] are known in literature. Compounds **31**, **38**, **48**, **53**, and **65** were obtained from commercial suppliers.

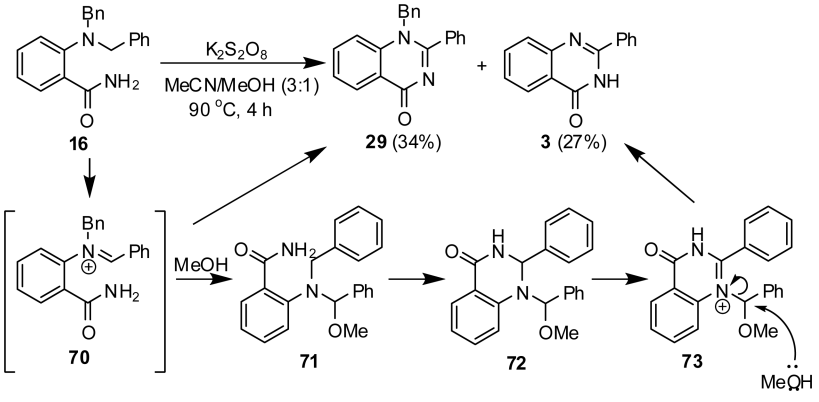
Typical Procedure for the Preparation of 2-(Benzylamino)-benzamides. A mixture of 2-aminobenzamide (1.0 mmol), TBAB (2.5 mmol), and benzyl bromide (1.2 mmol) in acetonitrile (4 mL) was heated at 90 °C for 6 h in a screw-capped reaction tube. After completion of the reaction, water (50 mL) was added to the reaction mixture. The mixture was then extracted with EtOAc (50 mL ×3), dried (Na_2SO_4), and concentrated under reduced pressure. Column chromatography [silica gel, EtOAc:hexane (1:4)] of the crude product yielded 2-(benzylamino)benzamides.

Typical Procedure for the Preparation of 2-Arylquinazolin-4(3H)-ones. A mixture of 2-(benzylamino)benzamides (0.5 mmol) and $K_2S_2O_8$ (1.0 mmol) in acetonitrile (5 mL) was heated at 90 °C for 3–4 h in a screw-capped reaction tube. After completion of the reaction (monitored by TLC analysis), water (25 mL) was added, and the resulting mixture was extracted with EtOAc (20 mL ×3) and then dried over anhydrous Na_2SO_4. Concentration under reduced pressure followed by chromatography of the crude [silica gel, 30% EtOAc:hexane] gave 2-arylquinazolin-4(3H)-ones.

Typical Procedure for the Preparation of 2-(Benzylamino)-benzenesulfonamides. A mixture of 2-aminobenzenesulfonamide (1.0 mmol), TBAB (2.5 mmol), and benzyl bromide (1.2 mmol) in acetonitrile (4 mL) was heated at 90 °C for 6 h in a screw-capped reaction tube. After completion of the reaction, water (50 mL) was added to the reaction mixture. The mixture was then extracted with EtOAc (50 mL ×3), dried (Na_2SO_4), and concentrated under reduced pressure. Column chromatography [silica gel, EtOAc:hexane (2:3)] of the crude product yielded 2-(benzylamino)benzenesulfonamide.

Typical Procedure for the Preparation of Sulfonyl Analogs of 2-Arylquinazolin-4(3H)-ones. A mixture of 2-(benzylamino)-benzenesulfonamide (0.5 mmol) and $K_2S_2O_8$ (1.0 mmol) in acetonitrile (5 mL) was heated at 90 °C for 12–16 h in a screw-capped reaction tube. After completion of the reaction (monitored by TLC analysis), water (50 mL) was added, and the resulting mixture was extracted with EtOAc (30 mL ×3), and then dried over anhydrous Na_2SO_4. Concentration under reduced pressure followed by chromatography of the crude [silica gel, 60% EtOAc:hexane] and/or

Scheme 10. Oxidative Functionalizations of *tert*-Benyzlamine 16 via Nucleophilic Addition to Iminium Ion 70



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recrystallization from EtOAc: dichloromethane (1:2) gave the title compound.

Typical Procedure for the Preparation of N-Aryl-N′-benzyl-1,2-diaminobenzenes. To a stirred suspension of 2-bromoaniline (2 mmol), and NaH (2 mmol), benzyl bromide (2.4 mmol) in DMF (10 mL) was added dropwise at room temperature under argon, and the reaction mixture was allowed to stir at room temperature for 3 h. After completion of the reaction, the reaction mixture was quenched with saturated aqueous NH_4Cl followed by addition of water (150 mL). The mixture was then extracted with EtOAc (50 mL ×4), and the organic layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography [silica gel, EtOAc:hexane (5:95)] of the crude yielded *N*-benzyl-2-bromoanilines.

A mixture of *N*-benzyl-2-bromoaniline (1.5 mmol), aniline (1.5 mmol), $Pd(OAc)_2$ (0.15 mmol), S-Phos (0.15 mmol), and Cs_2CO_3 (3.0 mmol) in anhydrous toluene (6 mL) was degassed for about 5 min and then heated at 110 °C for 16 h. The resulting mixture was filtered through a Celite bed, and the solid residue was washed with EtOAc (10 mL). Water (50 mL) was added to the filtrate and the aqueous layer was extracted with EtOAc (50 mL ×3). The combined organic layer was collected and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum, and the crude reaction mixture was purified by column chromatography on silica gel using 10% EtOAc:hexane as eluent, which upon drying under vacuum yielded the title compound.

Typical Procedure for the Preparation of 1,2-Diphenyl-1H-benzo[d]imidazoles. A mixture of *N*-benzyl-*N*-phenyl-1,2-diaminobenzene (0.5 mmol) and $K_2S_2O_8$ (1 mmol) in acetonitrile (5 mL) was heated at 90 °C for 4−6 h in a screw-capped reaction tube. After completion of the reaction, water (25 mL) was added, and the resulting mixture was extracted with EtOAc (25 mL ×3), and then dried over anhydrous Na_2SO_4. Concentration under reduced pressure followed by chromatography of the crude [silica gel, 20% EtOAc:hexane] 1,2-diphenyl-1H-benzo[*d*] imidazoles.

*Typical Procedure for the Preparation of 2-(Benzylamino)-benzoic Acids **48**−**52**.* The appropriate starting primary amine (2.0 mmol) and aldehyde (2.0 mmol) in MeOH (5 mL) were stirred for 30 min at room temperature. $NaBH_4$ (3.5 mmol) and NaOH (0.4 mmol) in H_2O (1 mL) were added to the reaction mixture, and the resulting solution was stirred for 6 h. The reaction was diluted with CH_2Cl_2 (200 mL) and washed with water (200 mL). The organic layer was filtered and dried over $MgSO_4$, and the solvent was removed. The crude solid was used in the next cyclization step without purification.

Typical Procedure for the Preparation of Benzoxazin-4-ones. A mixture of 2-(benzylamino)benzoic acids (0.5 mmol) and $K_2S_2O_8$ (1.0 mmol) in acetonitrile (5 mL) was heated at 90 °C for 8 h in a screw-capped reaction tube. After completion of the reaction (monitored by TLC analysis), water (50 mL) was added, and the resulting mixture was extracted with EtOAc (20 mL ×3) and then dried over anhydrous Na_2SO_4. Concentration under reduced pressure followed by chromatography of the crude [silica gel, 20% EtOAc:hexane] gave benzoxazin-4-ones.

*Typical Procedure for the Preparation of compounds **60** and **62**.* The appropriate starting primary amines [2-aminobenzamide or 4,5-dimethoxy-2-aminobenzoic acid, 1.0 mmol] and aldehyde (1.0 mmol) in CH_2Cl_2 or MeOH (2 mL) were stirred overnight at room temperature. Concentration followed by recrystallization from methanol gave the compounds.

*2-(Benzylamino)benzenesulfonamide (**4**).* Yield 98% (256 mg); Pale yellow solid; mp: 98−100 °C; ^{1}H NMR: δ 7.75 (dd, 7.7, 1.2 Hz, 1H), 7.40 (m, 2H), 7.23−7.25 (m, 4H), 6.70 (m, 2H), 4.49 (s, 2H); ^{13}C NMR: δ 145.1, 138.8, 133.4, 128.2, 126.7, 126.6, 124.6, 115.3, 112.4, 46.5; HRMS: obsd 263.0840 calcd 263.0854 for $C_{13}H_{15}N_2O_2S$ (M + H).

*2-(3-Methoxybenzylamino)benzamide (**5**).* Yield 99% (253 mg); Colorless solid; mp: 133−135 °C; ^{1}H NMR: δ 7.41 (dd, J = 8.4, 1.4 Hz, 1H), 7.24−7.29 (m, 3H), 6.97 (dd, J = 7.5, 0.6 Hz, 1H), 6.93 (s, 1H), 6.80 (dd, J = 8.1, 2.2, 1H), 6.59−6.66 (m, 2H), 4.43 (s, 2H), 3.80 (s, 3H); ^{13}C NMR: δ 172.07, 159.9, 150.1, 140.8, 113.5, 129.6, 128.2, 119.2, 114.8, 113.1, 112.5, 112.4, 55.2, 47.2; HRMS: obsd 257.1288, calcd 257.1290 for $C_{15}H_{17}N_2O_2$ (M + H).

*2-(3-(Trifluoromethyl)benzylamino)benzamide (**6**).* Yield 97% (285 mg); Pale brown solid; mp: 126−128 °C, ^{1}H NMR: δ 7.62 (s, 1H), 7.56 (d, J = 7.6, 1H), 7.52 (d, J = 7.7 Hz, 1H), 6.47 (dt, J = 8.0, 1.4 Hz, 2H), 7.26 (dt, J = 8.1, 1.4 Hz, 1H), 6.65 (dt, J = 8.0, 1.2 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 4.43 (s, 2H), 3.80 (s, 3H); ^{13}C NMR: δ 172.1, 149.9, 149.3, 140.3, 133.5, 130.2, 129.1, 128.3 (q, J = 261.0 Hz), 127.1, 125.5, 123.9, 123.7 (q, J = 16.0 Hz), 117.4, 115.3, 113.3, 112.2,46.6 ; HRMS: obsd 295.1049, calcd 295.1058 for $C_{15}H_{14}F_3N_2O$ (M + H).

*2-(3-(trifluoromethyl)benzylamino)benzenesulfonamide (**7**).* Yield 98% (323 mg); Pale brown solid; mp: 147−149 °C; ^{1}H NMR: δ 7.83 (dd, J = 7.9, 1.5 Hz, 1H), 7.62 (m, 2H), 7.45 (m, 2H), 7.33−7.39- (dt, J = 7.1, 1.4 Hz, 1H), 6.81 (dt, J = 7.2, 0.9 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 6.34 (br, 1H), 4.95 (s, 2H), 4.53 (d, J = 5.6 Hz, 2H); ^{13}C NMR: δ 145.1, 142.2, 134.6, 129.9, 129.6, 128.9 (q, J = 280.0 Hz), 127.1, 125.8(q, J = 13.0 Hz), 125.7, 124.1, 117.1, 113.0, 46.9 ; HRMS: obsd 330.0643 calcd 330.0650 for $C_{14}H_{13}F_3N_2O_2S$ (M^+).

*Methyl 4-((2-carbamoylphenylamino)methyl)benzoate (**9**).* Yield 99% (281 mg); Yellowish white solid; mp: 152−153 °C, ^{1}H NMR: δ 8.0 (d, J = 8.3 Hz, 2H), 7.45 (m, 3H), 7.25 (dt, J = 7.2, 1.5 Hz, 1H), 6.63 (t, J = 8 Hz, 1H), 6.59 (d, J = 8.4 Hz, 1H), 4.5 (s, 2H), 3.9 (s, 3H); ^{13}C NMR: δ 172.1, 166.9, 149.5, 144.4, 133.5, 129.9, 129.0, 128.3, 126.9, 115.5, 113.6, 112.6, 52.0, 47.0; HRMS: obsd 285.1235, calcd 285.1239 for $C_{16}H_{17}N_2O_3$ (M + H).

*2-(4-Chlorobenzylamino)benzenesulfonamide (**10**).* Yield 97% (287 mg); Pale yellow solid; mp: 148−150 °C; ^{1}H NMR: δ 7.83 (dd, 7.9, 1.5 Hz, 1H), 7.27−7.39 (m, 5H), 6.81 (dt, 8.0, 0.9 Hz, 1H), 6.70 (d, 8.2 Hz, 1H), 6.25 (s, 1H), 4.89 (s, 2H), 4.43 (d, 5.2 Hz, 2H); ^{13}C NMR: δ 145.2, 136.5, 134.6, 133.2, 129.0, 128.8, 124.1, 117.0, 113.0, 46.7; HRMS: obsd 297.0453 calcd 297.0465 for $C_{13}H_{14}ClN_2O_2S$ (M + H).

*2-(2-Bromobenzylamino)benzamide (**11**).* Yield 100% (304 mg); Pale yellow solid; mp: 162−164 °C; ^{1}H NMR: δ 7.58 (dd, J = 7.9, 1.1 Hz, 1H), 7.44 (dd, J = 7.8, 1.4 Hz 1H), 7.38 (td, J = 7.7, 0.8 Hz, 1H), 7.23−7.29 (m, 2H), 7.13 (dt, J = 7.4, 1.7 Hz, 1H), 6.63 (dt, J = 8.0, 1.0 Hz, 1H), 6.56 (d, J = 7.9 Hz, 1H), 4.51 (s, 2H); ^{13}C NMR: δ 172.0, 149.9, 137.7, 133.6, 132.7, 128.5, 128.4, 128.2, 127.5, 123.0, 115.1, 113.2, 112.3, 47.1; HRMS: obsd 305.0278, calcd 305.0290 for $C_{14}H_{14}BrN_2O$ (M + H).

*2-(3-Methylbenzylamino)benzenesulfonamide (**12**).* Yield 98% (270 mg); Colorless liquid; ^{1}H NMR: δ 7.74 (dd, J = 7.9, 1.4 Hz, 1H), 7.35 (dt, J = 7.3, 1.5 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.98 (m, 2H), 6.83 (dt, J = 8.1, 1.0 Hz, 1H), 6.78 (dd, J = 8.1, 0.8 Hz, 1H), 5.06 (t, 5.8 Hz, 1H), 4.87 (s, 2H), 4.02 (d, J = 6.2 Hz, 2H); ^{13}C NMR: δ 145.0, 138.3, 136.1, 134.2, 129.7, 128.6, 128.5, 128.3, 124.8, 121.6, 117.9, 117.7, 47.2, 21.2; HRMS: obsd 277.1011, calcd 277.1007 for $C_{14}H_{17}N_2O_2S$ (M + H).

*2-(3-Methoxybenzylamino)benzenesulfonamide (**13**).* Yield 97% (283 mg); Pale yellow semisolid; ^{1}H NMR: δ 7.82 (dd, J = 7.9, 1.6 Hz, 1H), 7.38 (dt, J = 7.3, 1.6 Hz, 1H), 7.28 (m, 1H), 6.94 (dd, J = 7.5, 0.5 Hz, 1H), 6.90 (d, J = 2 Hz, 1H), 6.82 (m, 1H), 6.78 (t, J = 7.8 Hz, 2H); ^{13}C NMR: δ 160.0, 159.7, 145.4, 139.7, 138.8, 134.5, 129.9, 129.6, 128.7, 124.1, 121.9, 119.2, 116.8, 114.9, 113.6, 113.1, 112.9, 112.6, 55.2, 47.4; HRMS: obsd 293.0947 calcd 293.0960 for $C_{14}H_{17}N_2O_3S$ (M + H).

*2-(4-Methylbenzylamino)benzenesulfonamide (**14**).* Yield 99% (273 mg); Colorless liquid; ^{1}H NMR: δ 7.75 (dd, J = 7.9, 1.4 Hz, 1H), 7.35 (dt, J = 7.3, 1.5 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.98 (m, 2H), 6.83 (dt, J = 8.1, 1.0 Hz, 1H), 6.78 (dd, J = 8.1, 0.8 Hz, 1H), 5.06 (t, 5.8 Hz, 1H), 4.87 (s, 2H), 4.02 (d, J = 6.2 Hz, 2H); ^{13}C NMR: δ 145.0, 138.3, 136.1, 134.2, 129.7, 128.6, 128.5, 128.3, 124.8, 121.6, 117.9, 117.7, 47.2, 21.2; HRMS: obsd 277.1007, calcd 277.1011 for $C_{14}H_{17}N_2O_2S$ (M + H).

*2-(4-Methoxybenzylamino)benzenesulfonamide (**15**).* Yield 97% (283 mg); Colorless liquid; ^{1}H NMR: δ = 7.74 (dd, J = 8.0, 1.5 Hz, 1H), 7.35 (dt, J = 7.3, 1.5 Hz, 1H), 7.10 (m, 2H), 6.77−6.84 (m, 4H), 5.03 (t, J = 5.0 Hz, 1H), 4.87 (s, 1H), 3.99 (d, J = 5.8 Hz, 2H), 3.80 (s,

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3H); ^{13}C NMR: δ 159.2, 145.0, 134.2, 130.4, 129.7, 129.2, 129.0, 128.6, 128.4, 128.2, 121.5, 117.9, 117.7, 114.2, 114.1, 114.0, 113.8, 55.3, 46.8; HRMS: obsd 293.0956, calcd 293.0960 for $C_{14}H_{17}N_2O_3S$ (M + H).

*2-(Dibenzylamino)benzamide (**16**).* Yield 98% (309 mg); Yellow solid; ^{1}H NMR: δ 8.21 (dd, J = 7.8, 1.7 Hz, 1H), 7.37 (dt, J = 7.4, 1.6 Hz, 1H), 7.29−7.31 (m, 6H), 7.23 (dt, J = 8.1, 0.9 Hz, 1H), 7.11−7.19 (m, 4H), 6.99 (d, J = 8 Hz, 1H), 4.14 (s, 4H), 5.40 (s, 2H); ^{13}C NMR: δ 168.4, 149.0, 137.0, 131.9, 131.8, 130.6, 129.5, 129.1, 128.7, 128,3, 128.2, 128.1, 127.8, 127.7, 127.3, 124.0, 123.9; HRMS: obsd 317.1644, calcd 317.1654 for $C_{21}H_{21}N_2O$ (M + H).

*2-(3-Methoxyphenyl)quinazolin-4(3H)-one (**18**).* Yield 72% (91 mg); Pale brown solid; mp: 195−197 °C, ^{1}H NMR: δ 11.53 (s, 1H), 8.33 (dd, J = 7.8, 0.8 Hz, 1H), 7.78−7.88 (m, 4H), 7.50−7.55 (m, 2H), 7.15 (dd, J = 8.3, 2.4 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR: δ 163.65, 160.19, 151.56, 149.44, 134.93, 134.17, 130.15, 128.06, 126.87, 126.36, 120.94, 119.53, 118.28, 112.25, 55.55; HRMS: obsd 253.0967, calcd 253.0972 for $C_{15}H_{13}N_2O_2$ (M + H).

*2-(3-(trifluoromethyl)phenyl)quinazolin-4(3H)-one (**19**).* Yield 77% (112 mg); Colorless solid; mp: 237−239 °C; ^{1}H NMR: δ 11.95 (s, 1H), 8.67 (s, 1H), 8.52 (d, J = 7.9 Hz, 1H), 8.40 (dd, J = 7.6, 0.8 Hz, 1H), 7.87−7.89 (m, 3H), 7.76 (t, J = 7.8 Hz 1H), 7.59 (dt, J = 7.6, 2.16 Hz, 1H); ^{13}C NMR: δ 162.09, 150.9, 148.4, 134.6, 133.6, 131.7, 129.8, 129.5, 129.2, 127.7, 127.6, 126.9(q, J = 278.0 Hz), 125.8, 125.0, 124.4(q, J = 14.0 Hz), 122.5, 121.1 ; HRMS: obsd 291.0739, calcd for 291.0740 for $C_{15}H_{10}F_3N_2O$ (M + H).

*3-(3-Trifluoromethylphenyl)-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide (**20**).* Yield 71% (116 mg); Colorless solid; mp: >300 °C, ^{1}H NMR: δ 12.61 (s, 1H) 8.20 (m, 2H), 8.16 (d, J = 7.0 Hz, 1H), 7.85 (t, J = 8.2 Hz, 1H), 7.75(d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H); ^{13}C NMR: δ 154.1, 136.2, 135.8, 133.7, 130.1, 129.7, 127.4(q, J = 230.0 Hz), 126.2(q, J = 10.0 Hz), 126.1,123.8, 121.9, 119.1 ; HRMS: obsd 327.0411, calcd 327.0415 for $C_{14}H_{10}F_3N_2O_2S$ (M + H).

*2-(4-Methylphenyl)quinazolin-4(3H)-one (**21**).* Yield 80% (94 mg); Colorless solid; mp: 181−183 °C, ^{1}H NMR: δ 8.32 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.2 Hz, 2H), 7.76−7.82 (m, 2H), 7.4 (dt, J = 8.1, 1.8 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR: δ 164.1, 151.9, 149.7, 142.1, 134.8, 130.0, 129.7, 127.9, 127.4, 126.5, 126.3, 120.7, 21.5; HRMS: obsd 237.1021, calcd 237.1028 for $C_{15}H_{13}N_2O$ (M + H).

*Methyl 4-(4-oxo-3,4-dihydroquinazolin-2-yl)benzoate (**22**).* Yield 90% (126 mg); Colorless solid; mp: 254−256 °C; ^{1}H NMR: δ 12.75 (s, 1H), 8.31 (d, J = 8.4 Hz, 2H), 8.17 (dd, J = 7.8,1.0 Hz, 1H), 8.11 (d, J = 8.4 Hz 2H), 7.85 (dt, J = 8.3, 1.4 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.56 (dt, J = 7.9, 0.8 Hz, 1H), 3.90 (s,3H); ^{13}C NMR: δ 166.1, 162.6, 151.9, 148.9, 137.3, 135.2, 132.2, 129.7, 128.6, 128.1, 127.5, 126.3, 121.6, 52.9; HRMS: obsd 281.0927, calcd 281.0926 for $C_{16}H_{13}N_2O_3$ (M + H); IR (KBr): 2922, 2851, 1732, 1673, 1282, 1114 cm^{-1}.

*3-(4-Chlorophenyl)-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide (**23**).* Yield 72% (105 mg); Pale yellow solid; mp: >300 °C; ^{1}H NMR: δ 8.07 (d, J = 7.0 Hz, 2H), 7.87 (dd, J = 7.9, 1.1 Hz, 1H), 7.73 (m, 3H), 7.62 (d, J = 8.0 Hz, 1H), 7.52 (dt, J = 7.8, 0.7 Hz, 1H); ^{13}C NMR: δ 153.7, 137.7, 135.3, 133.2, 130.5, 130.1, 128.9, 126.8, 123.3, 121.3, 118.4; HRMS: obsd 293.0141, calcd 293.0152 for $C_{13}H_{10}ClN_2O_2S$ (M + H).

*2-(2-Bromophenyl)quinazolin-4(3H)-one (**24**).* Yield 55% (83 mg); Light brown solid; mp: 175−177 °C; ^{1}H NMR: δ 9.95 (s, 1H), 8.33 (d, J = 8.0 Hz, 1H), 7.85 (m, 2H), 7.72−7.75 (m, 2H), 7.49−7.56 (m, 2H), 7.44 (t, J = 7.8 Hz, 1H); ^{13}C NMR: δ 161.9, 151.8, 148.9, 134.9, 134.8, 133.8, 132.1, 131.7, 129.0, 128.0, 126.5, 121.1, 120.7; HRMS: 300.9969, calcd 300.9971 for $C_{14}H_{10}BrN_2O$ (M + H).

*3-(m-Tolyl)-2H-benzo[e][1,2,4]thiadiazine 4-oxide 1,1-dioxide (**25**).* Yield 50% (72 mg); Brown solid; mp: 232 °C; ^{1}H NMR: δ 12.01 (s, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 7.3 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.61 (m, 3H), 7.44 (m, 2H); ^{13}C NMR: δ 157.2, 138.0, 137.6, 134.1, 132.6, 131.8, 130.5, 128.4, 127.7, 127.3, 124.1, 122.9, 116.0, 21.3; HRMS: obsd 289.0643, calcd 289.0647 for $C_{14}H_{13}N_2O_3S$ (M + H).

*3-(3-Methoxyphenyl)-2H-benzo[e][1,2,4]thiadiazine 4-oxide 1,1-dioxide (**26**).* Yield 62% (94 mg); Pale brown solid; mp: 226−228 °C; ^{1}H NMR: δ 7.90 (dd, J = 8.2, 1.2 Hz, 1H), 7.85 (m, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.9 Hz, 1H), 7.34 (m, 2H), 7.18 (ddd, J = 8.2, 2.6, 1.0 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR: δ 159.0, 156.8, 137.5, 134.1, 133.0, 129.8, 127.8, 124.1, 122.8, 122.3, 117.7, 116.0, 115.2, 55.8; HRMS: obsd 305.0590, calcd 305.0596 for $C_{14}H_{13}N_2O_4S$ (M + H)

*3-(p-Tolyl)-2H-benzo[e][1,2,4]thiadiazine 4-oxide 1,1-dioxide (**27**).* Yield 66% (95 mg); Pale brown solid; mp: 227−229 °C; ^{1}H NMR: δ 7.90 (d, J = 8.2 Hz, 2H), 7.80 (dd, J = 8.4, 0.7 Hz, 1H), 7.75 (d, J = 8.0 Hz, 2H), 7.61 (dt, J = 7.8, 1.1 Hz, 1H), 7.37 (d, 8.0 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR: δ 157.1, 142.4, 137.7, 134.1, 130.5, 129.1, 128.9, 127.7, 124.0, 122.9, 116.0, 21.5; HRMS: obsd 289.0638, calcd 289.0647 for $C_{14}H_{13}N_2O_3S$ (M + H); IR (KBr): 2670, 1590, 1392, 1323, 1186 cm^{-1}.

*3-(4-Methoxyphenyl)-2H-benzo[e][1,2,4]thiadiazine 4-oxide 1,1-dioxide (**28**).* Yield 51% (77 mg); Brown solid; mp: 213−215 °C; ^{1}H NMR: δ 7.79−7.89 (m, 5H), 7.60 (dt, J = 7.7, 1.1 Hz, 1H), 7.10 (dd, J = 7.0, 2.0 Hz, 2H), 3.85 (s, 3H), ^{13}C NMR: δ 162.5, 156.7, 137.8, 134.0, 132.9, 127.6, 123.9, 123.5, 123.0, 116.1, 114.0, 55.9; HRMS: obsd 305.0589, calcd 305.0596 for $C_{14}H_{13}N_2O_4S$ (M + H).

*N-Benzyl-2-phenylquinazolin-4(1H)-one (**29**).* Yield 95% (148 mg); Pale yellow semisolid; ^{1}H NMR: δ 8.46 (dd, J = 7.9, 1.4 Hz, 1H), 7.64 (dt, J = 8.2, 1.4 Hz, 1H), 7.55 (d, J = 8.1 Hz, 2H), 7.46−7.50 (m, 2H), 7.32−7.40 (m, 5H), 7.28 (d, J = 8.4 Hz, 1H) 7.10 (d, J = 7.0 Hz, 2H), 5.40 (s, 2H); ^{13}C NMR: δ 168.7, 163.2, 140.9, 135.1, 134.6, 133.9, 130.6, 129.3, 128.8, 128.6, 128.4, 128.0, 126.3, 125.5, 120.6, 116.7, 53.0; HRMS: obsd 313.1337, calcd 313.1341 for $C_{21}H_{17}N_2O$ (M + H).

*N1-Benzyl-N2-(3,5-dimethylphenyl)benzene-1,2-diamine (**32**).* Yield 55% (249 mg); Greenish yellow solid; mp: 79−81 °C; ^{1}H NMR: δ 7.34−7.37 (m, 5H), 7.15 (dd, J = 7.5, 1.4 Hz, 1H), 7.09 (dt, J = 7.5, 1.4 Hz 1H), 6.70−6.75 (m, 2H), 6.52 (s, 1H), 6.41 (s, 2H), 5.05 (s, 1H), 4.37 (s, 2H), 2.27 (s, 6H); ^{13}C NMR: δ 145.7, 143.9, 139.5, 129.2, 128.6, 128.5, 127.5, 127.28, 126.3, 125.1, 121.2, 117.3, 113.0, 111.2, 47.8, 21.4; HRMS: obsd 303.1855 calcd for 303.1861 for $C_{21}H_{23}N_2$ (M + H).

*N1-Benzyl-N2-(3,5-dimethylphenyl)-4-methylbenzene-1,2-diamine (**33**).* Yield 62% (294 mg); Light brown liquid; ^{1}H NMR: δ 7.25−7.37 (m, 5H), 6.99 (s, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.62 (d, J = 8.2 Hz, 1H), 6.52 (s, 1H), 6.42 (s, 2H), 4.36 (s, 2H), 2.28 (s, 6H), 2.25 (s, 3H); ^{13}C NMR: δ 145.7, 141.4, 139.8, 139.0, 128.3, 128.1, 127.2, 127.0, 126.8, 126.3, 121.2, 113.2, 111.4, 48.2, 21.4, 20.4; HRMS: obsd 317.2010 calcd 317.2018 for $C_{22}H_{25}N_2$ (M + H).

*N1-Benzyl-4-methyl-N2-(3-nitrophenyl)benzene-1,2-diamine (**34**).* Yield 72% (359 mg); Yellow solid; mp: 117−119 °C; ^{1}H NMR: δ 7.64 (dd, J = 8.0, 2.1 Hz, 1H), 7.51 (t, J = 2.2 Hz, 1H), 7.25−7.36 (m, 6H), 6.96−7.00 (m, 3H), 6.68 (d, J = 8.8 Hz, 1H), 5.45 (s, 1H), 4.36 (s, 2H), 2.28 (s, 3H); ^{13}C NMR: δ 149.3, 147.1, 149.9, 139.3, 129.8, 128.6, 128.0, 127.2 127.1, 126.5, 125.9, 120.3, 113.6, 111.9, 108.9, 48.1, 20.3; HRMS: obsd 334.1546, calcd 334.1556 for $C_{20}H_{20}N_3O_2$ (M + H).

*N1-Benzyl-4-fluoro-N2-(3-nitrophenyl)benzene-1,2-diamine (**35**).* Yield 76% (384 mg); Red solid; mp: 98−100 °C; ^{1}H NMR: δ 7.69 (dd, J = 8.0, 2.1 Hz, 1H), 7.58 (t, J = 2.2 Hz, 1H), 7.29−7.39 (m, 6H), 7.07 (dd, J = 8.1, 2.3 Hz, 1H), 6.92 (dd, J = 9.2, 2.8 Hz, 1H), 6.85 (dt, J = 8.4, 2.8 Hz, 1H), 6.68 (dd, J = 8.9, 5.2 Hz, 1H), 5.54 (s, 1H), 4.34 (s, 2H); ^{13}C NMR: δ155.8 (d, J = 236.0 Hz), 149.3, 145.9, 139.7, 139.7, 130.1, 128.7, 127.4 (d, J = 5.0 Hz), 121.0, 114.4, 113.0 (d, J = 22.0 Hz), s112.8, 112.7, 111.6, 111.4, 109.7, 48.6 ; HRMS: obsd 338.1318, calcd 338.1305 for $C_{19}H_{17}FN_3O_2$ (M + H).

*N1-Benzyl-N2-(3-fluorophenyl)-4-methylbenzene-1,2-diamine (**36**).* Yield 56% (257 mg); Brown solid; mp: 93−95 °C; ^{1}H NMR: δ 7.33 (m, 4H), 7.27−7.29 (m, 1H), 7.12−7.18 (m, 1H), 6.99 (d, J = 1.6 Hz, 1H), 6.93 (dd, J = 8.1, 1.4 Hz 1H), 6.65 (d, J = 8.1 Hz, 1H), 6.50−6.54 (m, 2H), 6.44 (td, J = 11.2, 2.2 Hz, 1H), 5.2 (br, 1H), 4.35 (s, 1H), 2.26 (s, 3H); ^{13}C NMR: δ 164.0(d, J = 242.0 Hz),147.9, 147.8,

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141.7, 139.5, 130.3, 130.2, 128.6, 128.3, 127.5, 127.3, 127.2, 127.0(d, J = 4.0 Hz),126.2, 111.7, 110.7, 110.6, 105.5(d, J = 22 Hz), 101.9, 101.7, 48.2; HRMS: obsd 307.1601, calcd 307.1611 for $C_{20}H_{20}FN_2$ (M + H).

*N1-Benzyl-4-fluoro-N2-phenylbenzene-1,2-diamine (**37**).* Yield 64% (280 mg); Green liquid; ^{1}H NMR: δ 7.27−7.35 (m, 8H), 6.88−6.98 (m, 3H), 6.66−6.74 (m, 2H), 5.29 (br, 1H), 4.34 (s, 2H); ^{13}C NMR: δ 156.0 (d, J = 235.0 Hz), 144.1, 139.2, 138.3, 130.9, 130.8, 129.7, 128.0 (d, J = 3.0 Hz), 127.3, 120.5, 116.7, 115.8, 115.5, 113.7, 113.6, 112.6, 112.5, 110.3 (d, J = 22.0 Hz), 109.14, 108.9, 103.4, 48.9; HRMS: obsd 293.1450, calcd 293.1454 for $C_{19}H_{18}FN_2$ (M + H).

*1-(3,5-Dimethylphenyl)-2-phenyl-1H-benzo[d]imidazole (**41**).* Yield 87% (130 mg); Brown solid; ^{1}H NMR: δ 7.90 (d, J = 7.9 Hz, 1H), 7.63 (d, J = 6.8 Hz, 2H), 7.30−7.36 (m, 5H), 7.26 (s, 1H), 7.11 (s, 1H), 6.94 (s, 2H), 2.36 (s, 6H); ^{13}C NMR: δ 139.7, 129.9, 129.9, 128.2, 123.2, 122.9, 119.6, 110.6, 21.2; HRMS: obsd 299.1535, calcd 299.1548 for $C_{21}H_{19}N_2$ (M + H).

*1-(3,5-Dimethylphenyl)-6-methyl-2-phenyl-1H-benzo[d]-imidazole (**42**).* Yield 90% (140 mg); Light brown solid; mp: 136−139 °C; ^{1}H NMR: δ 7.76 (d, J = 8.24 Hz, 1H), 7.60−7.62 (dd, J = 8.3,1.8 Hz, 2H), 7.30−7.35 (m, 3H), 7.16 (dd, J = 8.2, 1.1 Hz, 1H), 7.12 (d, J = 0.6 Hz, 1H), 7.02 (t, J = 0.8 Hz, 1H), 6.93 (d, J = 0.4 Hz, 2H), 2.47 (s, 3H), 2.35 (s, 6H); ^{13}C NMR: δ 151.8, 140.9, 139.6, 137.6, 136.9, 133.2, 130.2, 129.2, 129.1, 128.1, 125.0, 124.4, 119.2, 110.3, 21.6, 21.1; HRMS: obsd 313.1695, calcd 313.1705 for $C_{22}H_{21}N_2$ (M + H).

*6-Methyl-1-(3-nitrophenyl)-2-phenyl-1H-benzo[d]imidazole (**43**).* Yield 95% (156 mg); Reddish brown solid; mp: 136−139 °C, ^{1}H NMR: δ 8.34 (d, J = 7.3 Hz, 1H), 8.27 (t, J = 2 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 8.4, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.32−7.39 (m, 3H), 7.22 (d, J = 8.2 Hz, 1H), 7.05 (s, 1H); ^{13}C NMR: δ 151.8, 149.0, 141.0, 138.3, 136.6, 134.2, 133.5, 130.8, 129.8, 129.4, 129.2, 128.6, 125.2, 123.2, 122.2, 119.8, 109.7, 21.8; HRMS: obsd 330.1232, calcd 330.1243 for $C_{20}H_{16}N_3O_2$ (M + H); IR (KBr): 1613, 2924, 2854, 1536, 1464, 1348 cm^{-1}.

*6-Fluoro-1-(3-nitrophenyl)-2-phenyl-1H-benzo[d]imidazole (**44**).* Yield 80% (133 mg); Reddish brown solid; mp: 198−201 °C; ^{1}H NMR: δ 8.36 (d, J = 8.2 Hz, 1H), 8.25 (t, J = 2.0 Hz, 2H), 7.86 (dd, J = 8.8, 4.8 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.50−7.52 (dd, J = 8.2, 2.1 Hz, 1H), 7.34−7.44 (m, 3H), 7.15−7.18 (dt, J = 9.4, 2.4 Hz, 1H), 6.96 (dd, J = 8.4, 2.3 Hz, 1H); ^{13}C NMR: δ δ 160.3 (d, J = 240.0 Hz), 152.9, 149.0, 139.4, 137.9, 136.7, 136.5, 133.2, 131.0, 130.1, 129.3, 128.9, 128.7, 123.5, 122.1, 121.2(d, J = 10.0 Hz), 112.0 (d, J = 25.0 Hz), 96.8 (d, J = 29.0 Hz); HRMS: obsd 334.0983, calcd 334.0992 for $C_{19}H_{13}FN_3O_2$ (M + H); IR (KBr): 1621, 1537, 1475, 1349, 1156 cm^{-1}.

*1-(3-Fluorophenyl)-6-methyl-2-phenyl-1H-benzo[d]imidazole (**45**).* Yield 96% (145 mg); Reddish brown solid; mp: 173−175 °C; ^{1}H NMR: δ 8.00 (d, J = 8.2 Hz, 1H), 7.68 (d, J = 7.3 Hz, 2H), 7.54−7.60 (m, 1H), 7.48 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 9.1 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.13−7.18 (m, 2H), 7.08 (s, 1H), 2.50 (s, 3H); ^{13}C NMR: δ 163.1 (d, J = 250.0 Hz), 149.8, 136.4, 136.3, 135.2, 131.8, 131.7, 131.5, 129.8, 127.1, 125.2, 123.7, 123.4 (d, J = 3.0 Hz),117.6, 117.2(d, J = 21.0 Hz), 115.0 (d, J = 23.0 Hz),110.7, 21.9; HRMS: 303.1296, calcd 303.1298 for $C_{20}H_{16}FN_2$ (M + H).

*6-Fluoro-1,2-diphenyl-1H-benzo[d]imidazole (**46**).* Yield 85% (122 mg); Bright yellow solid; mp: 120−122 °C; ^{1}H NMR: δ 7.83 (dd, J = 8.7, 4.5 Hz, 1H), 7.50−7.57 (m, 5H), 7.35−7.38 (m, 1H), 7.30−7.34 (m, 4H), 7.10 (dt, J = 8.9, 2.5 Hz, 1H), 6.95 (dd, J = 8.6, 2.8 Hz, 1H); ^{13}C NMR: δ 160.1 (d, J = 239.0 Hz), 153.1, 159.2, 137.4, 137.2, 136.6, 130.0, 129.6, 129.5, 129.2, 128.6, 128.4, 127.1, 120.6, 120.5, 111.3 (d, J = 25.0 Hz), 97.2 (d, J = 28.0 Hz); HRMS: obsd 289.1132; calcd 289.1141 for $C_{19}H_{14}FN_2$ (M + H).

*2-(Benzylamino)-4,5-dimethoxybenzoic Acid (**49**).* Yield 98% (281 mg); Pale brown solid; ^{1}H NMR: δ 7.45 (s, 1H), 7.34−7.42 (m, 4H), 7.29−7.32 (m, 1H), 6.1 (s, 1H), 4.50 (s, 1H), 3.84 (s, 3H), 3.76 (s, 3H); ^{13}C NMR: δ 173.0, 156.0, 149.0, 139.6, 138.9, 128.7, 127.2, 126.9, 113.9, 99.9, 95.0, 56.3, 55.6, 47.4; HRMS: obsd 288.1229, calcd 288.1236 for $C_{16}H_{18}NO_4$ (M + H).

*4,5-Dimethoxy-2-(4-methylbenzylamino)benzoic Acid (**51**).* Yield 97% (292 mg); Light brown solid; mp: 163−165 °C; ^{1}H NMR: δ 7.44 (s, 1H), 7.27 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 6.12 (s, 1H), 4.45 (s, 2H), 3.84 (s, 3H), 3.78 (s, 3H), 2.36 (s, 3H); ^{13}C NMR: δ 173.0, 156.0, 149.0, 139.6, 138.9, 128.7, 127.2, 126.9, 113.9, 99.9, 95.0, 56.3, 55.6, 47.4; HRMS: obsd 302.1388, calcd 302.1392 for $C_{17}H_{20}NO_4$ (M + H).

*2-(4-Hydroxy-3-methoxybenzylamino)-4,5-dimethoxybenzoic Acid (**52**).* Yield 96% (319 mg); Yellow solid; mp: 175−177 °C; ^{1}H NMR: δ 7.44 (s, 1H), 7.31 (d, J = 8.5 Hz, 1H), 6.90 (d, J = 8.6 Hz, 2H), 6.13 (s, 1H), 4.42 (s, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.79 (s, 3H); ^{13}C NMR: δ 173.1, 158.8, 156.0, 149.0, 139.5, 130.8, 128.2, 114.15, 113.9, 100.0, 95.0, 56.4, 55.6, 55.3, 46.9; HRMS: obsd 334.1289, calcd 334.1291 $C_{17}H_{20}NO_6$ (M + H).

*6,7-Dimethoxy-2-phenyl-4H-benzo[d][1,3]oxazin-4-one (**54**).* Yield 60% (85 mg); Colorless solid; mp: 217−219 °C; ^{1}H NMR: δ 8.30 (dd, J = 8.5 Hz, 1.5 Hz, 2H), 7.50−7.59 (m, 4H), 7.14 (s, 1H), 4.06 (s, 3H), 4.02 (s, 3H); ^{13}C NMR: δ 159.5, 156.6, 156.4, 149.7, 143.3, 132.3, 130.4, 128.8, 128.7, 109.6, 108.1, 107.6, 56.5, 56.4, 53.4; HRMS: obsd 284.0914, calcd 284.0923 for $C_{16}H_{14}NO_4$ (M + H).

*6,7-Dimethoxy-2-(4-nitrophenyl)-4H-benzo[d][1,3]oxazin-4-one (**55**).* Yield 35% (57 mg); Green solid; mp: 209−211 °C; ^{1}H NMR: δ 8.45 (d, J = 7.0 Hz, 2H), 8.35 (d, J = 6.9 Hz, 2H), 7.58 (s, 1H), 7.15 (s, 1H), 4.02 (s, 3H), 3.99 (s, 3H); ^{13}C NMR: δ 158.7, 156.6, 154.3, 150.5, 142.6, 136.1, 128.8, 123.9, 109.3, 108.4, 107.7, 56.6, 56.5; HRMS: obsd 328.0686, calcd 328.0695 for $C_{16}H_{12}N_2O_6$ (M^+).

*6,7-Dimethoxy-2-p-tolyl-4H-benzo[d][1,3]oxazin-4-one (**56**).* Yield 30% (45 mg); Colorless solid; ^{1}H NMR: δ 8.18 (d, J = 8.2 Hz, 2H), 7.57 (s, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.12 (s, 1H), 4.05 (s, 3H), 4.01(s, 3H), 2.46 (s, 3H); ^{13}C NMR: δ 159.6, 156.8, 156.4, 149.5, 143.5, 143.0, 129.5, 128.0, 127.6, 109.5, 108.0, 107.6, 56.5, 56.4, 21.6; HRMS: obsd 298.1071, calcd 298.1079 for $C_{17}H_{16}NO_4$ (M + H); IR (KBr): 2918, 2579, 1645, 1521, 1231 cm^{-1}.

*2-(Benzylideneamino)benzamide (**60**).* Yield 60% (134 mg); Colorless solid; mp: 200−202 °C; ^{1}H NMR: δ 8.48 (s, 1H), 8.35 (dd, J = 7.9, 1.6 Hz, 1H), 7.90 (dd, J = 7.8, 1.7 Hz, 2H), 7.53−7.59 (m, 4H), 7.40 (dt, J = 7.8, 1.2 Hz, 1H), 7.10 (dd, J = 7.9,1.0 Hz, 1H); ^{13}C NMR: δ 167.8, 161.6, 149.8, 135.3, 134.4, 133.0, 132.9, 132.4, 131.6, 129.7, 129.1, 129.0, 127.9, 126.7, 126.0, 118.7, 117.4, 116.3, 113.8; HRMS: obsd 225.1021, calcd 225.1028 for $C_{14}H_{13}N_2O$ (M + H).

*2-(Benzylideneamino)-4,5-dimethoxybenzoic Acid (**62**).* Yield 80% (228 mg); Bright yellow solid; mp: 204−206 °C; ^{1}H NMR: δ 8.70 (s, 1H), 7.89 (d, J = 8.5 Hz, 2H), 7.79 (s, 1H), 7.53−7.63 (m, 3H), 6.92 (s, 1H), 3.98 (s, 3H), 3.92 (s, 3H); ^{13}C NMR: δ 192.4, 167.2, 158.1, 155.6, 153.3, 149.3, 148.0, 140.7, 134.4, 133.8, 133.2, 129.7, 129.4, 129.0, 128.7, 117.6, 113.4, 112.9, 100.8, 99.2, 98.7, 56.3, 55.8; HRMS: obsd 286.1072, calcd 286.1079 for $C_{16}H_{16}NO_4$ (M + H).

*N-(4-Bromobenzyl)-4-chloroaniline (**66**).* Yield 98% (288 mg); Pale yellow solid; mp: 82−84 °C; ^{1}H NMR: δ 7.45 (d, J = 6.7 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 6.50 (d, J = 6.8 Hz, 2H); ^{13}C NMR: δ 146.3, 138.0, 131.7, 129.1, 128.9, 122.1, 121.2, 113.9, 47.7; HRMS: obsd 295.9849, calcd 295.9842 for $C_{13}H_{12}BrClN$ (M + H).

*N-(4-Chlorophenyl)benzamide (**67**).* Yield 70% (81 mg); White solid; mp: 181−183 °C; ^{1}H NMR: δ 7.88(m, 2H), 7.8 (s, 1H), 7.57−7.64 (m, 3H), 7.50 (m, 2H), 7.35 (dd, J = 6.7, 2.0 Hz, 2H); ^{13}C NMR: δ 165.6, 136.5, 134.6, 132.0, 129.5, 129.1, 128.8, 126.9, 121.5; HRMS: obsd 232.0535, calcd 232.0529 for $C_{13}H_{11}ClNO$ (M + H).

*4-Bromo-N-(4-chlorophenyl)benzamide (**68**).* Yield 45% (70 mg); Brown solid; mp: 186−188 °C; ^{1}H NMR: δ 7.80 (s, 1H), 7.76 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.1 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), ^{13}C NMR: δ 164.7, 136.2, 133.4, 132.1, 129.8, 129.1, 128.6, 126.8, 121.5; HRMS: obsd 308.9548, calcd 308.9556 for $C_{13}H_9BrClNO$ (M^+).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01872.

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

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Notes

The authors declare no competing financial interest.

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