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Synthesis of Polysubstituted 2-Aminoimidazoles via Alkene-Diamination of Guanidine with Conjugated α-Bromoalkenones

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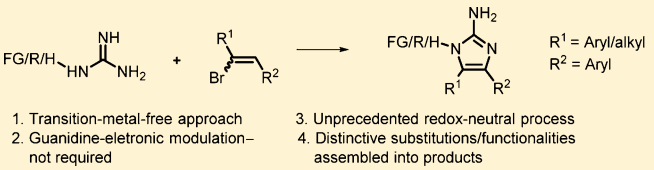
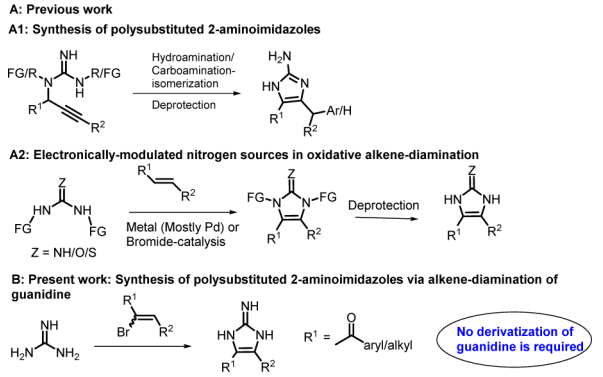
Supporting Information

ABSTRACT: A step-economical access to polysubstituted aminoimidazoles has been accomplished via alkene vicinal C−N bonds formation of 2-bromo-2-alkenones with guanidine avoiding its NH-protection/derivatization prerequisite for electronic modulation. The approach has excellent substrate scope, is amenable to diverse guanidine-containing substrates, and introduces distinctive substitutions/functionalities into aminoimidazole core. It is also applicable to preparation of fused-imidazoles. The reaction involves a tandem pathway of aza-Michael addition, S_N2, and a unique redox-neutral process, as evident by spectroscopic study and control experiments.



2-Aminoimidazoles are omnipresent in the marine-sponge alkaloids[1] and therapeutic/bioactive agents.[2] 2-Aminoimidazole core has an interesting hydrogen-bond-donor/acceptor patterns, and with varied poly substitutions/functionalities exhibit diverse bioactivities, selectivity in enzyme-inhibition, and important physicochemical properties.[3] In addition, 2-aminoimidazoles are employed as synthones,[4] organocatalysts,[5] metal−ligands,[6] and anion-recognizing agents.[7] Therefore, the synthesis of highly functionalized 2-aminoimidazole core is of increasing demand. There are two major approaches for preparation of multisubstituted 2-aminoimidazoles,[8,9] (1) the condensation of α-haloketone with an acetylated guanidine or condensation of an α-aminoketone with cyanamide,[9,10] and (2) functionalization of imidazole scaffold via protection, C2-amination, introducing substituents and deprotection.[11] While the first approach is incompetent in introducing important functional-diversity and uses unstable precursors, the latter method requires multistep reactions. Moreover, the assembly of particular substituents/functionalities into 2-aminoimidazoles requires postmodification or use of starting substrates which are not readily available. 5-Aroyl substituted 2-aminoimidazole has been prepared by an olefinic-amination of cyanamide with α-azido functionalized chalcone.[12] Recently reported methods to access substituted 2-aminoimidazoles from propargyl guanidine represent a remarkable route (Scheme 1A1). They include lanthanide-mediated intramolecular hydroamination−isomerization of propargyl guanidine prepared in situ by amine-addition to propargyl cyanamide,[13] a sequence of guanylation of propargylamines with *N*,*N*′-bis-Boc-protected thiourea, Ag(I)-mediated 5-exo-dig heterocyclization, deprotection and isomerization,[14] and a method of Pd-catalyzed carboamination with aryl triflates.[15] Here, we report an approach of direct assembly of guanidine into a conjugated α-bromoketone via alkene vicinal C−N bonds formation, which provides 4-aryl/alkyl and 5-acyl substituted and *N*-functionalized 2-aminoimidazoles (Scheme 1B).

Scheme 1. Previous and Present Work



Intramolecular transfer of various nitrogen sources, such as guanidine,[16] urea,[17] sulfamide,[18] oxalimide,[17] to alkene via oxidative vicinal diamination with transition-metal (mostly Pd) or halogen-catalysis is an active area of research (Scheme 1A2).[19−21] The electronic property of the involved nitrogen atoms as sufficiently nucleophilic in suitable NH-protected forms (e.g., Tos, Boc, Cbz) has been found to be crucial.[22] In addition, the process is dependent on nature of alkene, majorly preferred for terminal alkene.[23] The use of free guanidine in alkene-diamination has never been known, which would produce the 2-aminoimidazole core.[24] In contrast, the reaction of guanidine with α,β-unsaturated carbonyls produces 2-aminopyrimidines and is considered as a useful method.[25] Recently, Hajra et al. reported an alkene-diamination of conjugated enone with 2-aminobenzthiazole.[26] Notably, guanidine in reaction with 1,3-diyne undergoes 1,3-diamination.[27] In present work, free guanidine has been rendered as

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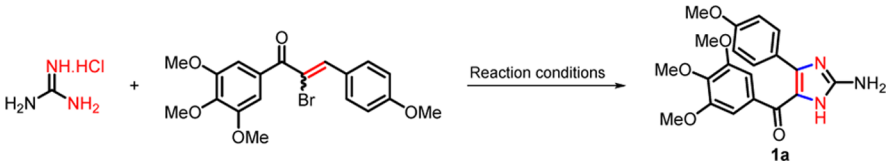
Table 1. Evaluation of Reagents and Conditions[a]



entry	guanidine (equiv)[c]	base (equiv)	solvent (anhyd, 5 mL)	oxidant (1.5 equiv)	yield (%)[b]
1	2	NaH (2.2)	1,4-dioxane		40
2	2	No base	1,4-dioxane		NR
3	2	KO^{t}Bu (2.2)	1,4-dioxane		30
4	2	LiOH (2.2)	1,4-dioxane		25
5	2	K_2CO_3 (2.2)	1,4-dioxane		45
6	2	Na_2CO_3 (2.2)	1,4-dioxane		35
7	2	Cs_2CO_3 (2.2)	1,4-dioxane		40
8	2	DBU (2.2)	1,4-dioxane		20
9	2	DIPEA (2.2)	1,4-dioxane		5
10	3	K_2CO_3 (3.5)	1,4-dioxane		51
11	3.5	K_2CO_3 (4)	1,4-dioxane		51
12	3	K_2CO_3 (3.5)	1,4-dioxane	MnO_2	70
13	3	K_2CO_3 (3.5)	1,4-dioxane	DDQ	5
14	3	K_2CO_3 (3.5)	1,4-dioxane	$K_2S_2O_8$	20
15	3	K_2CO_3 (3.5)	1,4-dioxane	TBHP[d]	33
16[e]	3	K_2CO_3 (3.5)	MeCN	MnO_2	40
17	3	K_2CO_3 (3.5)	DMF	MnO_2	35
18	3	K_2CO_3 (3.5)	DMSO	MnO_2	30
19[e]	3	K_2CO_3 (3.5)	EtOH	MnO_2	50
20[f]	3	K_2CO_3 (3.5)	PEG 400	MnO_2	20
21	3	K_2CO_3 (3.5)	toluene	MnO_2	NR
22	3	K_2CO_3 (3.5)	dioxane-H_2O (5:1)	MnO_2	30

[a]Substrates, reagents and conditions: α-bromochalcone (0.25 mmol) and others as mentioned in the table, 100 °C. [b]Yield for maximum conversion in optimum time. [c]Guanidine·HCl received commercially was used without pre-neutralization. [d]TBHP (in decane). [e]Reaction temperature is 80 °C. [f]2 mL solvent.

effective substrate for alkene vicinal C−N bonds formation with conjugated α-bromoketone.

The mechanism of alkene-diamination by metal or bromide catalysis[19,21] involves a related pathway. The reaction undergoes via vicinal amino-metalation/bromination, and subsequent alkyl C−N bond formation through S_N2 (a concomitant transient metal-oxidation taking place in metal-catalysis). The mechanistic path incited us to identify a substrate suitable for diamination of free guanidine in a transition-metal-free process. We considered that α,β-unsaturated ketone bearing α-bromo functionality could be an effective substrate. Vicinal diamination of guanidine can be obtained by aza-Michael addition and subsequently S_N2. It is worth to mention that there is no report of aza-Michael addition[28] of guanidine to α,β-unsaturated ketone and, in fact, *N*-acetylguanidine in a reaction with 2,3-alkenone undergoes exclusively 1,2-addition for imine formation.[9] Therefore, in the reaction of guanidine with 2-bromo-2,3-alkenone, a crucial task is to accomplish switching from imine-forming route to a pathway of aza-Michael addition−S_N2−oxidation that can produce 2-aminoimidazole.

We initiated the study for the reaction of α-bromochalcone (E-isomer) with guanidine hydrochloride pretreated with NaH base. Desired 4-aryl-5-benzoyl-2-aminoimidazole was obtained in 40% yield and, however, the side product 2-aminopyrimidine was also produced in 30% yield. The reaction was found to be noninfluenced by stereoisomeric (*E*/*Z*) aspect of α-bromochalcone, Therefore, *E*/*Z*-isomer as obtained in preparation following a reported method[29] was utilized as substrate in next experiments. We investigated various bases (Table 1, entry 1−9). K_2CO_3 was found to be best. On the other hand, addition of a Lewis acid, e.g., $FeCl_3$, $ZrCl_4$, or $In(OTf)_3$, resulted in enhanced formation of 2-aminopyrimidine (40−45% yields, data not shown) and decreased production of 2-aminoimidazole (25−33% yields), evidently indicating a preference for imine-forming route. Increased yield of the substituted 2-aminoimidazole as well as diminished formation of side products including 2-aminopyrimidine was observed with an optimum enhanced dilution of the reaction mixture along with elevated temperature. Pretreatment of guanidine·HCl with base was found unnecessary. Optimal quantity of guanidine and potassium carbonate (3.0 and 3.5 equiv., respectively) improved slightly the yield (entries 5, 10, and 11). Interestingly, use of an oxidizing agent MnO_2 boosted the formation of the desired 2-aminoimidazole in significantly higher yield (entry 10 vs 12). However, other tested oxidizing agents were found to be nonefficient for the reaction. Screening of solvents indicated superior efficiency of 1,4-dioxane. Importantly, 2-aminopyrimidine side product was obtained in trace quantity (3% yield) under optimized conditions. During these investigations, Li et al. reported a reaction of diaryl-amidine and chalcone with $FeCl_3/I_2$-catalysis producing imidazoles, which involved a related pathway.[30] The transformation is limited to NH-arylated arylamidine and low-yielding for alkylamidine, clearly indicating the necessity of sufficient nucleophilicity of nitrogen for C−N bond formations. We evaluated the feasibility of such $FeCl_3/I_2$-catalysis for the present reaction, however, the

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substrates remained nearly intact and the desired product did not form. This implies that the exceptional behavior of free guanidine as poorly nucleophilic is responsible for guiding the reactions away from alkene-diamination pathway. A reaction of guanidine with chalcone replacing α-bromochalcone under optimized conditions was performed. Desired 2-aminoimidazole did not form and, conversely, 2-aminopyrimidine was obtained in considerable quantity (40% yield). These indicate that α-bromoalkenone as an effective substrate as well as optimized conditions enabled the chemoselective vicinal C−N bond formation with free guanidine.

Structure of the product was confirmed by spectroscopies and X-ray crystallographic analysis (Figure 1).

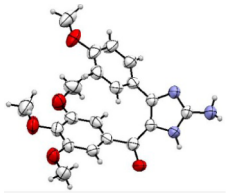

Figure 1. ORTEP diagram of 4-(4-methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1*H*-imidazole-2-amine (**1a**).

With optimized conditions, we next investigated the generality of the protocol and preparation of varied 2-aminoimidazole derivatives. We were pleased to find that the method was found to be flexible in accommodating a variety of substrates (Table 2).

2-Bromoalkenones containing electron-donating or withdrawing functionalities were compatible. In general, electron donating functionalities provided relatively higher yields compared to the electron withdrawing groups. Heterocyclic α-bromochalcones were congruent to this protocol. Aliphatic ketone substrate underwent diamination smoothly. The presence of biologically relevant (hetero)aryl motifs in the substrates were also compatible in the reaction.

We were then interested to investigate the method's applicability to versatile guanidine-containing motifs (Table 3). Delightfully, the reaction underwent smoothly with *N*-amino/cyano/aryl-substituted guanidines. Interestingly, the reaction for these nonsymmetrical guanidines was found to be chemoselective and only one product was obtained. The structure of these regioisomeric products were unambiguously confirmed by their spectroscopic data. The products indicated that functionalized amine-nitrogen site underwent Michael addition with chalcones. The products obtained using these guanidine-containing motifs are biologically important. In case of 2-aminobenzimidazole also, desired imidazole-fused scaffold was obtained, albeit the formation of fused pyrimidine via imine-forming route in significant quantity was observed. Such ring-annulation of alkene is attractive and has potential application, since 2-aminoimidazole motif is omnipresent in marine-based NPs, drugs and bioactive agents, and the fused heterocyclic products are biologically important.[31] The protocol proved also to be amenable to a scale-up synthesis (investigated up to 5 mmol) without significant decrease in yield. In contrast to the conventional/classical methods known for synthesis of the title compounds, the present approach is step-economical and convenient, uses easily accessible and economical starting substrates, and has an excellent substrate scope. More importantly, substitutions/functionalities distinctive from literature have been introduced easily into the 2-aminoimidazole ring.

We were then interested in gaining insight into the possible mechanism. Under optimized conditions or lowering the temperature, none of the intermediate formed in isolable quantity. In correlation with literature, it is expected that vicinal C−N bonds formation occurred possibly via Michael addition−S_N2 process.[30,32] A control reaction without MnO_2 under otherwise identical conditions (entry 10 vs 12, Table 1) produced desired product, 4-(4-methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1*H*-imidazole-2-amine (**1a**) in significant yield (51%). Another control reaction without MnO_2 in the second most effective solvent EtOH produced also the desired product (**1a**) in 30% yield. These clearly suggest that the conversion of imidazoline to imidazole, subsequent to vicinal C−N bonds formation, did not involve direct dehydrogenative oxidation by MnO_2. In the reaction, chalcones were obtained in trace quantity, ruling out the possibility of intermolecular hydrogen transfer from imidazoline to bromochalcones. On the other hand, interestingly, use of MnO_2 significantly enhanced the yield of 2-aminoimidazole (51 to 70% yield, entry 10 vs 12). Mass spectrometry of crude mixture obtained at interval time for multiple experiments was studied (see SI). The characteristic peaks agreeably indicated the formation of pertinent intermediates (**A**, **B**, **C**; Scheme 2) and an unprecedented internal redox-neutral process involved in the generation of 4-aryl-5-aroyl-1*H*-imidazole-2-amine. MnO_2 oxidizes methanetriamine to generate back guanidine. For conversion of imidazoline to imidazole, this redox-neutral process is distinctive, while the dehydrogenative oxidation[29] is the usual method.

In conclusion, we have developed an unprecedented alkene-vicinal C−N bonds formation of conjugated α-bromoketone with guanidine avoiding its electronic-modulation, which affords an efficient route to poly substituted/functionalized 2-aminoimidazoles. The reaction proceeds via a tandem pathway of aza-Michael addition, S_N2, and a unique redox-neutral process, a new pathway switched from literature-known route of producing 2-aminopyrimidines. For synthesis of the title compounds, the present approach has several attributes, step-economy, convenient procedure, excellent substrate scope, introduction of distinctive substitutions/functionalities into 2-aminoimidazole core, and use of economical/easily accessible starting substrates and reagents. Moreover, the present strategy can provide impetus of investigating alkene-diamination of other frequently used nitrogen sources without their electronic modulation.

■ EXPERIMENTAL SECTION

General Information. ATR and IR (KBr) Microscope spectrometer was used to record Infrared (IR) spectra. ^{1}H NMR spectra were measured on a 400 MHz spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard in $CDCl_3$/DMSO-d_6 integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dt = doublet of triplet, dd = doublet of doublet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were measured on a 100 MHz spectrometer with complete proton decoupling. Chemical shifts were reported in ppm. High-resolution mass spectra (HRMS) were performed on a high-resolution LCMS/MS instrument with "QTOF" mass analyzer. For thin-layer chromatography (TLC) analysis throughout this work, commercially supplied precoated TLC plates (silica gel 60 GF434, 0.43 mm) were used. The products were purified by column chromatography silica gel 100−200 (silica gel 100−200 mesh, neutral,

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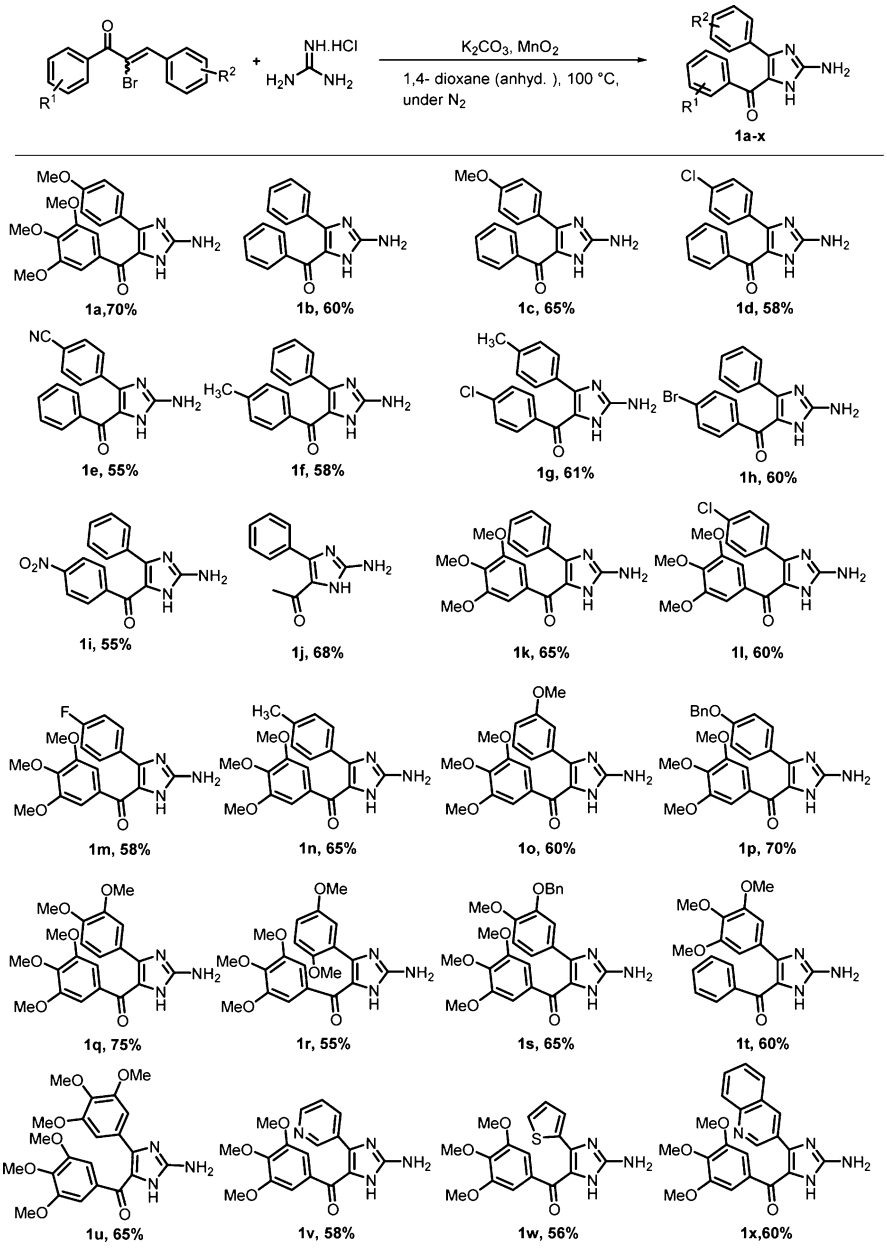
Table 2. Substrate Scope[a,b]



[a]Substrates, reagents and conditions: α-bromochalcone (0.5 mmol), guanidine HCl (3 equiv), K_2CO_3 (3.5 equiv), MnO_2 (1.5 equiv), 1,4-dioxane (anhyd.,8 mL), 100 °C. [b]Yield for maximum conversion in optimum time.

spherical).The starting materials and solvents were used as received from commercially without further purification.

*Representative Experimental Procedure for Synthesis of 4-(4-Methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1a**).* α-Bromochalcone (*E*/*Z*-mixture, 0.5 mmol), guanidine·HCl (1.5 mmol, 143 mg, 3 equiv), K_2CO_3 (1.75 mmol, 242 mg, 3.5 equiv), and manganese dioxide (0.75 mmol, 65 mg, 1.5 equiv) were taken under nitrogen in an oven-dried sealed tube equipped with a rubber septum and magnetic bar. Dioxane (anhyd., 8 mL) was added under nitrogen. The tube was then sealed. The mixture was stirred at 100 °C and the reaction was monitored by TLC. The reaction after 16 h was allowed to cool to room temperature and diluted with EtOAc-MeOH (1:1, 60 mL). The resultant mixture was filtered through Celite and concentrated under reduced pressure. The column chromatographic purification of crude mass was performed on silica gel (100–200 mesh) partially deacidified by passing triethylamine (1–4 mL) using MeOH-EtOAc (5:95) as eluting solvent. It provided 4-(4-methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1*H*-imidazole-2-amine (**1a**) (134 mg, 70%).

Products (**1b–x**, Table 2) were prepared following this representative procedure.

Products (**2a–f**, Table 3) were also prepared following this representative procedure. In the method, guanidine-containing motifs were used in place of guanidine·HCl.

*Characterization Data of the Synthesized Compounds (**1a–x**, **2a–f**). 4-(4-Methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1a**).* Yellow solid; 134 mg, 70%, mp >200 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.91 (s, *NH*), 7.16 (d, *J* = 8.1 Hz, 2H), 6.7 (s, 2H), 6.67 (d, *J* = 8.3 Hz, 2H), 5.98 (s, 2H), 3.68 (s, 3H), 3.62 (s, 3H), 3.54 (s, 6H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)): δ 181.8, 158.6, 152.8, 152.1, 148.5, 139.6, 133.8, 130.4, 127.4, 121.3, 112.6, 106.2, 59.9, 55.4, 55.0 ppm; IR (KBr): ν_{max} 3422, 2922, 1654, 1561, 1514, 1387, 1250, 1123 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{22}N_3O_5$ $[M+H]^+$ 384.1559, found: 384.1550.

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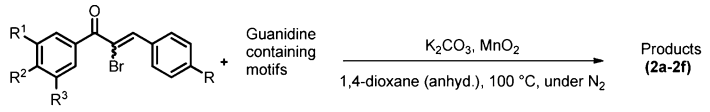
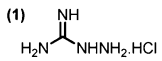
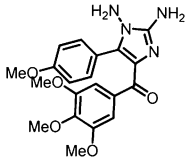
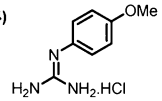
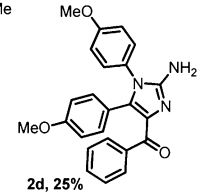
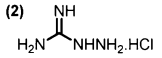
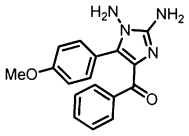
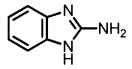
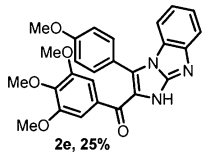
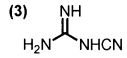
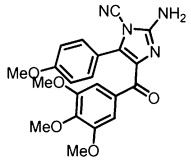
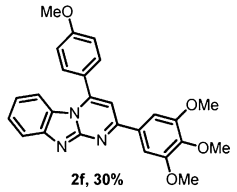
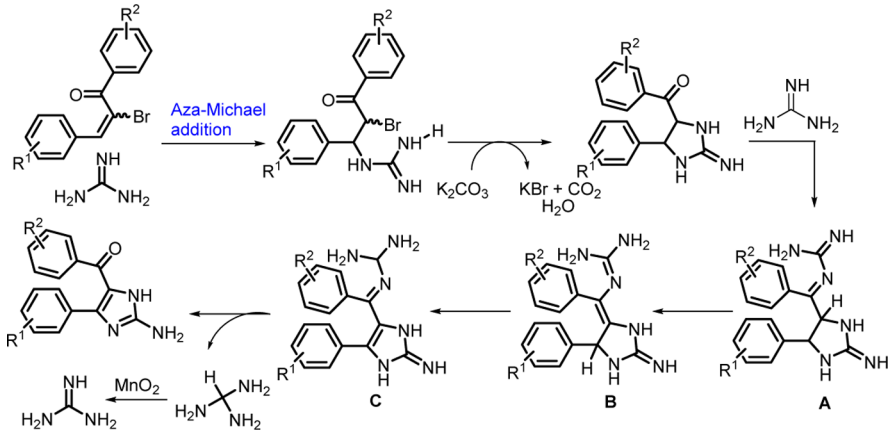
Table 3. Substrate Scope[a,b]



Guanidine containing motifs	Products	Guanidine containing motifs	Products
(1) 	 2a, 65%	(4) 	 2d, 25%
(2) 	 2b, 60%	(5) 	 2e, 25%
(3) 	 2c, 60%		 2f, 30%

[a]Substrates, reagents and conditions: α-bromochalcone (0.5 mmol), guanidine containing motifs (3 equiv), K_2CO_3 (3.5 equiv), MnO_2 (1.5 equiv), 1,4-dioxane (anhyd., 8 mL), 100 °C. [b]Yield for maximum conversion in optimum time.

Scheme 2. Plausible Mechanism



*5-Benzoyl-4-phenyl-1H-imidazole-2-amine (**1b**).* Yellow solid; 79 mg, 60%; mp >200 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.01 (s, *NH*), 7.39−7.34 (m, 3H), 7.24−7.07 (m, 7H), 6.02 (s,2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 183.6, 153.4, 149.4, 139.5, 135.1, 131.3, 129.6, 129.1, 128.2, 127.9, 127.8, 122.4 ppm; IR(KBr): ν_{max} 3425, 3061, 1650, 1551, 1528, 1381, 1299, 1171 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{16}H_{14}N_3O$ $[M+H]^+$ 264.1137, found: 264.1138.

*5-Benzoyl-4-(4-methoxyphenyl)-1H-imidazole-2-amine (**1c**).* Yellow solid; 95 mg, 65%; mp >200 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.83 (s, *NH*), 7.40 (d, *J* = 7.08 Hz, 2H), 7.35 (dd, *J* = 7.4 Hz, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.21(dd, *J* = 7.6 Hz, *J* = 7.6 Hz, 2H), 6.63 (d, *J* = 8.8 Hz, 2H), 5.98 (s,2H), 3.68 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 183.3, 159.2, 153.3, 149.4, 139.7, 131.1, 130.9, 128.9, 128.3, 127.4, 121.9, 113.3, 55.5 ppm; IR (KBr): ν_{max} 3409, 2997, 1648, 1543, 1508, 1383, 1247, 1170 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{16}N_3O_2$ $[M+H]^+$ 294.1242, found: 294.1245

*5-Benzoyl-4-(4-chlorophenyl)-1H-imidazole-2-amine (**1d**).* Yellow solid; 86 mg, 58%; mp >200 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.05 (s, *NH*), 7.43- 7.38 (m, 3H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.23 (dd, *J* = 7.2 Hz, *J* = 7.1 Hz, 2H), 7.13(d, *J* = 8.0 Hz, 2H), 6.05 (s,2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 183.5, 153.4, 147.9, 139.5, 133.9, 132.5,131.4, 131.2, 129.1, 128.3, 127.8, 122.5 ppm; IR (KBr): ν_{max} 3442, 2923, 1662, 1546, 1527, 1379, 1264, 1180, 738 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{16}H_{13}{}^{35}ClN_3O$ $[M+H]^+$ 298.0747, found: 298.0741.

*5-Benzoyl-4-(4-cyanophenyl)-1H-imidazole-2-amine (**1e**).* Yellow solid; 79 mg, 55%; mp >200 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.19 (s, *NH*), 7.54 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.44−7.39 (m, 3H), 7.24 (dd, *J* = 7.9 Hz, *J* = 7.4 Hz, 2H), 6.09 (s,2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 183.7, 153.5, 146.8, 139.7, 139.3, 131.7, 130.2, 129.1, 128.4, 123.2, 119.3, 110.0 ppm; IR (KBr): ν_{max} 3423, 3074, 2225, 1654, 1552, 1510, 1373, 1268, 1172

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cm^{-1}; HRMS (ESI) m/z: calcd for $C_{17}H_{13}N_4O$ $[M+H]^+$ 289.1089, found: 289.1082.

*5-(4-Methylbenzoyl)-4-phenyl-1H-imidazole-2-amine (**1f**).* Yellow solid; 80 mg, 58%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.96 (s, *N*H), 7.32 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.14−7.07 (m, 3H), 6.99 (d, J = 7.7 Hz, 2H), 6.00 (s, 2H), 2.24 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 183.4, 153.2, 148.7, 141.3, 136.8, 135.2, 129.6, 129.3, 128.8, 127.8, 122.3, 21.4 ppm; IR (KBr): ν_{max} 3432, 3296, 3060, 1654, 1579 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{17}H_{16}N_3O$ $[M+H]^+$ 278.1293, found: 278.1201.

*5-(4-Chlorobenzoyl)-4-(p-tolyl)-1H-imidazole-2-amine (**1g**).* Yellow solid; 95 mg, 61%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.01 (s, *N*H), 7.38 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.15 (d, J = 7.7 Hz, 2H), 6.91 (d, J = 7.7 Hz, 2H), 6.08 (s, 2H), 2.22 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 181.9, 153.6, 150.1, 138.4, 137.3, 135.8, 132.1, 130.9, 129.6, 128.4, 128.2, 122.1, 21.2 ppm; IR (KBr): ν_{max} 3441, 3246, 3094, 1654, 1576, 753 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{17}H_{15}ClN_3O$ $[M+H]^+$ 312.0903, found:312.0749.

*5-(4-Bromobenzoyl)-4-phenyl-1H-imidazole-2-amine (**1h**).* Yellow solid; 103 mg, 60%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.09 (s, *N*H), 7.34 (d, J = 7.9 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 7.2 Hz, 2H), 7.19−7.08 (m, 3H), 6.12 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 181.5, 153.1, 149.5, 138.1, 134.4, 130.5, 129.2, 127.4, 127.2, 124.1,121.7 ppm; IR (KBr): ν_{max} 3433, 3412, 3261, 3059, 2924, 1651, 1576 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{13}BrN_3O$ $[M+H]^+$ 342.0242, found: 342.0028.

*5-(4-Nitrobenzoyl)-4-phenyl-1H-imidazole-2-amine (**1i**).* Yellow solid; 85 mg, 55%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.24 (s, *N*H), 7.94 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 7.19−7.11 (m, 3H), 7.04 (dd, J = 7.2 Hz, J = 7.1 Hz, 2H), 6.256 (s, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 180.9, 154.3, 151.7, 148.4, 145.6, 134.7, 130.3, 129.8, 128.2, 127.8, 123.2, 122.6 ppm; IR (KBr): ν_{max} 3416, 3250, 3059, 1653, 1552, 1533 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{13}N_4O_3$ $[M+H]^+$ 309.0987, found: 309.0978.

*5-Acetyl-4-phenyl-1H-imidazole-2-amine (**1j**).* Yellow solid; 68 mg, 68%; mp: charred at 138−140 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.89 (s, *N*H), 7.65 (d, J = 6.8 Hz, 2H), 7.41−7.33 (m, 3H), 5.88 (s,2H), 2.08 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 157.1, 134.4, 133.2, 133.0, 32.6 ppm; IR (KBr): ν_{max} 3440, 3224, 3063, 1646, 1574, 1538, 1385, 1323 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{11}H_{12}N_3O$ $[M+H]^+$ 202.0980, found: 202.0981.

*4-Phenyl-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1k**).* Yellow solid; 115 mg, 65%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 7.23 (d, J = 7.0 Hz, 2H), 7.16−7.09 (m, 3H), 6.74 (s, 2H), 6.02 (s,2H), 3.61 (s, 3H), 3.52 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.9, 153.2, 152.6, 140.5, 135.2, 134.2, 129.7, 127.8, 127.7, 107.0, 60.4, 55.9 ppm; IR (KBr): ν_{max} 3433, 3278, 2937, 1660, 1584, 1549, 1531, 1375, 1234, 1126 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{19}H_{20}N_3O_4$ $[M+H]^+$ 354.1454, found: 354.1458.

*4-(4-Chlorophenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1l**).* Yellow solid; 116 mg, 60%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.13 (s, *N*H), 7.21 (d, J = 7.0 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 6.68 (s, 2H), 6.04 (s,2H), 3.62 (s, 3H), 3.56 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.7, 153.4, 152.7, 147.8, 140.5, 134.3, 132.5, 131.2, 127.7, 122.5, 106.9, 60.6, 56.1 ppm; IR (KBr): ν_{max} 3437, 3301, 3235, 2936, 1646, 1583, 1561, 1533, 1382, 1236, 1125, 732 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{19}H_{19}{}^{35}ClN_3O_4$ $[M+H]^+$ 388.1064, found: 388.1056.

*4-(4-Fluorophenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1m**).* Yellow solid; 108 mg, 58%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.11 (s, *N*H), 7.20 (s, 2H), 6.91 (dd, J = 8.2 Hz, J = 8.1 Hz, 2H), 6.66 (s, 2H), 6.03 (s,2H), 3.59 (s, 3H), 3.54 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 187.7, 166.7 (d, J_{C-F} = 244 Hz), 158.1, 157.4, 152.9, 145.1, 138.9, 136.3 (d, $J_{C-C-C-F}$ = 8 Hz), 127.1, 119.4 (d, J_{C-C-F} = 21 Hz), 111.6, 65.2, 60.8 ppm; IR (KBr): ν_{max} 3449, 3318, 2924, 1634, 1581, 1558, 1507, 1144, 1222, 1124 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{19}H_{19}FN_3O_4$ $[M+H]^+$ 372.1359, found: 372.1356.

*4-(p-Tolyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1n**).* Yellow solid; 120 mg, 65%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.97 (s, *N*H), 7.09 (d, J = 7.6 Hz, 2H), 6.90 (d, J = 7.6 Hz, 2H), 6.68 (s, 2H), 5.98 (s,2H), 3.60 (s, 3H), 3.51 (s, 6H), 2.19 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 187.3, 158.1, 157.4, 153.9, 145.2, 141.8, 139.1, 137.4, 134.3, 133.0, 126.9, 111.7, 65.2, 60.7, 25.9 ppm; IR (KBr): ν_{max} 3437, 3316, 2938, 1643, 1580, 1538, 1383, 1235, 1125 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{20}H_{22}N_3O_4$ $[M+H]^+$ 368.1610, found: 368.1601.

*4-(3-Methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1o**).* Yellow solid; 115 mg, 60%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.06 (s, *N*H), 7.06 (dd, J = 7.8 Hz, J = 7.7 Hz, 1H), 6.89 (d, J = 7.2 Hz, 1H), 6.71- 6.64 (m, 4H), 6.03 (s,2H), 3.60 (s, 3H), 3.52 (s, 6H), 3.49 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.6, 158.8, 153.4, 152.6, 148.9, 140.4, 136.8, 134.4, 128.8, 122.4, 121.9, 114.6, 114.5, 106.9, 60.3, 55.9, 55.1 ppm; IR (KBr): ν_{max} 3427, 3225, 2923, 1644, 1553, 1499, 1376, 1233, 1124 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{20}H_{22}N_3O_5$ $[M+H]^+$ 384.1559, found: 384.1555.

*4-(4-(Benzyloxy)phenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1p**).* Yellow solid; 161 mg, 70%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.93 (s, *N*H), 7.39−7.30 (m, 5H), 7.15 (d, J = 8.1 Hz, 2H), 6.75 (d, J = 8.2 Hz, 2H), 6.69 (s, 2H), 5.98 (s,2H), 5.03 (s, 2H), 3.61 (s, 3H), 3.51 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 181.8, 157.7, 152.8, 152.0, 148.3, 139.7, 136.9, 133.8, 130.4, 128.3, 127.7, 127.3, 121.2, 113.5, 106.3, 69.0, 59.9, 55.4 ppm; IR (KBr): ν_{max} 3422, 3230, 2923, 1656, 1552, 1514, 1386, 1232, 1129 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{26}H_{26}N_3O_5$ $[M+H]^+$ 460.1872, found: 460.1865.

*4-(3,4-Dimethoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1q**).* Yellow solid; 155 mg, 75%, mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.95 (s, *N*H), 6.94 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.72 (s, 2H), 6.61 (s, 1H), 6.00 (s,2H), 3.69 (s, 3H), 3.60 (s, 3H), 3.53 (s, 6H), 3.42 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.5, 153.3, 152.6, 149.2, 148.8, 148.0, 140.3, 134.5, 128.1, 121.9, 113.8, 111.5, 106.9, 60.4, 56.0, 55.9, 55.3 ppm; IR (KBr): ν_{max} 3432, 3245, 2939, 1640, 1540, 1514, 1253, 1231, 1126 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{21}H_{24}N_3O_6$ $[M+H]^+$ 414.1665, found: 414.1665.

*4-(2,5-Dimethoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1r**).* Yellow solid; 114 mg, 55%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.03 (s, *N*H), 6.89 (d, J = 2.9 Hz, 1H), 6.69 (dd, J = 8.9 Hz, J = 2.9 Hz, 1H), 6.64 (s, 2H), 6.48 (d, J = 8.9 Hz, 1H), 5.95 (s, 2H), 3.64 (s, 3H), 3.56 (s, 3H), 3.52 (s, 6H), 3.16 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.5, 152.8, 152.4, 151.5, 149.9, 143.3, 139.3, 134.1, 125.3, 122.7, 115.7, 114.1, 110.8, 105.2, 59.7, 55.2, 54.6 ppm; IR (KBr): ν_{max} 3432, 3245, 2922, 1639, 1580, 1503, 1252, 1230, 1124 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{21}H_{24}N_3O_6$ $[M+H]^+$ 414.1665, found: 414.1657.

*4-(3-(Benzyloxy)-4-methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1s**).* Yellow solid; 159 mg, 65%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.04 (s, *N*H), 7.39−7.29 (m, 5H), 6.98 (dd, J = 8.4 Hz, J = 1.6 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 6.70 (s, 2H), 6.55 (s, 1H), 6.01 (s,2H), 4.51 (s, 2H), 3.68 (s, 3H), 3.55 (s, 3H), 3.49 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.9, 153.1, 152.6, 149.1, 147.1, 140.3, 137.1, 134.3, 128.9, 128.4, 127.9, 122.2, 115.3, 111.8, 106.8, 69.9, 60.5, 56.1, 55.9 ppm; IR (KBr): ν_{max} 3432, 3322, 2936, 1639, 1583, 1508, 1384, 1253, 1134 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{27}H_{28}N_3O_6$ $[M+H]^+$ 490.1978, found: 490.1970.

*5-Benzoyl-4-(3,4,5-trimethoxyphenyl)-1H-imidazole-2-amine (**1t**).* Yellow solid; 106 mg, 60%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.98 (s, *N*H), 7.41 (d, J = 7.2 Hz, 2H), 7.35 (dd, J = 7.4 Hz, J = 7.4 Hz, 1H), 7.20 (dd, J = 7.6 Hz, J = 7.6 Hz, 2H), 6.56 (s, 2H), 6.06 (s,2H), 3.58 (s, 3H), 3.50 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 183.3, 153.3, 152.3, 149.1, 139.7, 137.5, 131.3, 130.3, 129.2, 128.1, 122.3, 107.2, 60.4, 55.8 ppm; IR (KBr): ν_{max} 3397, 3316, 2923, 1654, 1587, 1500, 1377, 1229, 1125 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{19}H_{20}N_3O_4$ $[M+H]^+$ 354.1454, found: 354.1447.

*4-(3,4,5-Trimethoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1u**).* Yellow solid; 144 mg, 65%; mp >200 °C; ^1H

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NMR (400 MHz, DMSO-d_6): δ 11.05 (s, *N*H), 6.70 (s, 2H), 6.47 (s, 2H), 6.05 (s,2H), 3.60 (s, 3H), 3.58 (s, 3H), 3.55 (s, 6H), 3.52 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.6, 153.4, 152.6, 152.4, 140.3, 137.5, 134.6, 130.8,122.3, 107.2, 106.8, 60.3, 60.2, 55.9, 55.8 ppm; IR (KBr): ν_{max} 3422, 3175, 2928, 1638, 1582, 1505, 1381, 1232, 1123 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{26}N_3O_7$ $[M+H]^+$ 444.1771, found: 444.1764.

*4-(Pyridin-3-yl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1v**).* Yellow solid; 103 mg, 58%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.24 (s, *N*H), 8.39 (s, 1H), 8.33 (dd, *J* = 4.8 Hz, *J* = 1.5 Hz, 1H), 7.59 (d, *J* = 7.3 Hz, 1H), 7.17 (dd, *J* = 7.7 Hz, *J* = 4.8 Hz, 1H), 6.75 (s, 2H), 6.10 (s,2H), 3.62 (s, 3H), 3.56 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.7, 153.6, 152.7, 149.9, 148.5, 140.5, 136.5, 134.0, 131.2, 122.9, 106.9, 60.4, 56.1 ppm; IR (KBr): ν_{max} 3329, 3178, 2926, 1650, 1609, 1568, 1412, 1339,1301,1230, 1124 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{18}H_{19}N_4O_4$ $[M+H]^+$ 355.1406, found: 355.1396.

*4-(Thiophen-2-yl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1w**).* Yellow solid; 101 mg, 56%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 10.84 (s, *N*H), 7.46 (d, *J* = 4.8 Hz, 1H), 7.42 (d, *J* = 2.7 Hz, 1H), 6.93−6.89 (m, 3H), 6.05 (s,2H), 3.72 (s, 6H), 3.71 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 181.2, 152.5, 142.1, 140.0, 137.6,134.4, 127.4, 127.1, 126.8, 120.5, 105.9, 60.1, 55.7 ppm; IR (KBr): ν_{max} 3245, 2959, 1637, 1500, 1380, 1263, 1124 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{18}N_3O_4S$ $[M+H]^+$ 360.1018, found: 360.1014.

*4-(Quinolin-3-yl)-5-(3,4,5-trimethoxybenzoyl)-1H-imidazole-2-amine (**1x**).* Yellow solid; 121 mg, 60%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 11.32 (s, *N*H), 8.74 (d, *J* = 1.4 Hz, 1H), 8.13 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.68 (dt, *J* = 6.9 Hz, *J* = 1.2 Hz, 1H), 7.52 (dd, *J* = 7.2 Hz, *J* = 7.2 Hz, 1H), 6.78 (s, 2H), 6.15 (s,2H), 3.48 (s, 6H), 3.33 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.4, 153.2, 152.1, 150.5, 146.2, 139.7, 135.2, 133.7, 129.4, 128.3, 128.0, 127.9, 126.7, 126.6, 106.4, 59.5, 55.4 ppm; IR (KBr): ν_{max} 3432, 3260, 2938, 1639, 1580, 1540, 1503, 1414, 1252, 1231, 1125 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{21}N_4O_4$ $[M+H]^+$ 405.1563, found: 405.1555.

*4-(4-Methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-N-amino-imidazole-2-amine (**2a**).* Yellow amorphous solid; 129 mg, 65%; mp: 92−94 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 7.40 (d, *J* = 8.7 Hz, 2H), 7.33 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.72 (s,2H), 5.43 (s,2H), 3.77 (s, 3H), 3.75 (s, 6H), 3.68 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 186.6, 159.3, 152.3, 149.6, 140.7, 135.9, 134.8, 132.5, 129.8, 122.2, 113.4, 108.2, 60.5, 56.3, 55.6 ppm; IR (KBr): ν_{max} 3473, 3327, 2929, 1692, 1582, 1503, 1249, 1125 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{23}N_4O_5$ $[M+H]^+$ 399.1668, found: 399.1663.

*5-Benzoyl-4-(4-methoxyphenyl)-N-amino-imidazole-2-amine (**2b**).* Yellow amorphous solid; 92 mg, 60%; mp: 153−155 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.49−7.45 (m, 3H), 7.39 (dd, *J* = 7.6 Hz, *J* = 7.2 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 5.74 (s,2H), 5.45 (s,2H), 3.79 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 187.9, 159.4, 149.5, 139.9, 135.9, 132.5, 131.5, 130.3, 129.7, 127.9, 122.0, 113.4, 55.6 ppm; IR (KBr): ν_{max} 3332, 3203, 2925, 1610, 1553, 1362, 1275, 1259, 1177 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{17}N_4O_2$ $[M+H]^+$ 309.1351, found:309.1346.

*4-(4-Methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-N-cyano-imidazole-2-amine (**2c**).* Yellow amorphous solid; 129 mg, 60%; mp:147−149 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 7.14 (d, *J* = 8.7 Hz, 2H), 6.81 (s, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 3.69 (s, 3H), 3.59 (s, 3H), 3.58 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 183.8, 163.2, 160.3, 152.7, 141.3, 132.4, 131.6, 120.9, 118.9, 113.7, 107.2, 60.5, 56.2, 55.8 ppm; IR (KBr): ν_{max} 3427, 3330, 3147, 2203, 2158, 1626, 1566, 1504, 1098, 1252 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{20}N_4O_5$ $[M+Na]^+$ 431.1332, found: 431.1326.

*5-Benzoyl-4-(4-methoxyphenyl)-N-(4-methoxyphenyl)-imidazole-2-amine (**2d**).* Yellow amorphous solid; 63 mg, 25%; mp: charred at 168−170 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 8.03 (dd, *J* = 8.5 Hz, *J* = 1.4 Hz, 2H), 7.52−7.48 (m, 1H), 7.41 (dd, *J* = 7.7 Hz, *J* = 7.2 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.8 Hz, 2H), 5.53 (s,2H), 3.75 (s, 3H), 3.69 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 188.2, 159.4, 159.0, 149.5, 139.6, 135.7, 133.2, 132.4, 131.7, 130.3, 129.9, 128.1, 127.8, 122.5, 115.0, 113.4, 55.8, 55.4 ppm; IR (KBr): ν_{max} 3454, 3295, 2958, 1639, 1566, 1512, 1498, 1248 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{21}N_3O_3$ $[M+Na]^+$ 422.1481, found: 422.1468.

*4-(4-Methoxyphenyl)-5-(3,4,5-trimethoxybenzoyl)-1H-benzo[d]-imidazo[1,2-a]imidazole (**2e**).* Yellow amorphous solid; 57 mg, 25%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 12.00 (s, *N*H), 7.58 (d, *J* = 8.6 Hz, 2H), 7.46−7.44 (m, 3H), 7.32 (dd, *J* = 7.8 Hz, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.09−7.04 (m, 3H), 3.84 (s, 3H), 3.78 (s, 6H), 3.72 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 187.4, 159.9, 152.5, 148.1, 141.3, 134.0, 132.0, 127.9, 125.1, 124.6, 121.7, 120.2, 114.1, 112.2, 108.4, 60.6, 56.4, 55.7 ppm; IR (KBR): ν_{max} 3063, 2939, 1634, 1611, 1579, 1469, 1251, 1234, 1124 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{24}N_3O_5$ $[M+H]^+$ 458.1716, found: 458.1716.

*4-(4-Methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)benzo[4,5]-imidazo[1,2-a]pyrimidine (**2f**).* Yellow amorphous solid; 33 mg, 30%; mp >200 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 7.82 (d, *J* = 8.12 Hz, 1H), 7.79 (s, 1H), 7.75 (d, *J* = 8.6 Hz, 2H), 7.69 (s, 2H), 7.45 (dd, *J* = 7.8 Hz, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 7.09 (dd, *J* = 8.2 Hz, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 3.94 (s, 6H), 3.93 (s, 3H), 3.77 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 161.1, 160.0, 153.2, 151.5, 149.5, 144.9, 140.3, 131.7, 130.3, 127.2, 125.5, 124.5, 120.7,119.2, 114.5, 114.4, 105.4, 105.0, 60.2, 56.1, 55.5 ppm; IR (KBr): ν_{max} 2937, 1596, 1496, 1251, 1125 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{24}N_3O_4$ $[M+H]^+$ 442.1767, found: 442.1759.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b03021.

Mass spectra for mechanistic investigation and NMR spectra (PDF)

X-ray crystallographic data for product **1a** (CCDC 1509458)[33] (CIF)

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Notes

The authors declare no competing financial interest.

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