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One-Pot Synthesis of 2,4,5-Trisubstituted Imidazoles via [2 + 2 + 1] Cycloannulation of 1,3-Bishet(aryl)-monothio-1,3-diketones, α-Substituted Methylamines and Sodium Nitrite through α-Nitrosation of Enaminones

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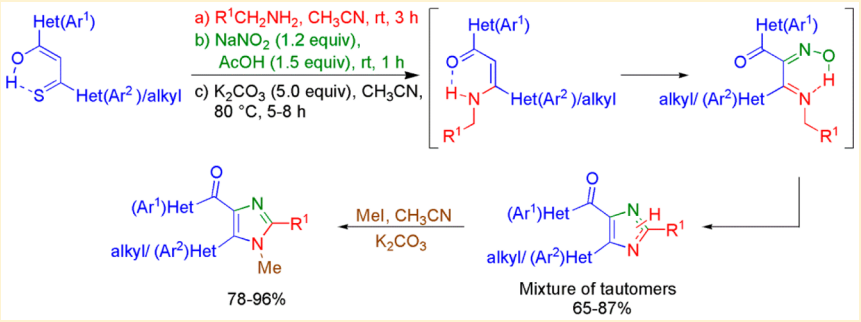
Supporting Information



ABSTRACT: An efficient one-pot synthesis of a series of diversely functionalized trisubstituted 4(5)het(aroyl)-2,5(4)-het(aryl)/alkylimidazoles from readily available 1,3-bishet(aryl)monothio-1,3-diketones has been reported. This novel sequential one-pot, three step protocol, wherein three new carbon nitrogen bonds are formed in contiguous fashion, involves in situ generation of enaminones by reaction of monothio-1,3-diketones with α-substituted methylamines, followed by their α-nitrosation with sodium nitrite and subsequent base mediated intramolecular heterocyclization of the resulting α-hydroxyiminoimines to trisubstituted imidazoles in high yields under mild conditions. These newly prepared 4(5)-het(aroyl)-5(4)-het(aryl)/alkylimidazoles are shown to exist as tautomeric mixture, however, their subsequent alkylation with methyl iodide in the presence of potassium carbonate affords 1-*N*-methy-2,5-bishet(aryl)-4-het(aroyl)imidazoles in highly regioselective fashion in most of the cases. Synthesis of few 4(5)-(2-hydroxyphenyl)-2,5(4)-substituted imidazoles, which are known to be good coordinating ligands, has also been reported. A probable mechanism for the formation of these imidazoles from hydroxyiminoimine intermediates has also been suggested.

INTRODUCTION

Imidazole heterocycles are regarded as privileged structural motifs,[1] which are prevalent in several highly significant biomolecules, including essential amino acids, histidine, histamine,[2a] biotin and bioactive natural products such as pilocarpine alkaloids.[1b,2] They also constitute core structure of many therapeutic agents[3a] and marketed drugs such as losartan,[3] cimetidine, dacarbazine, metronidazole, eprosartan.[3] Several of the imidazole derivatives display broad range of biological activities, acting as antibacterial agents,[4a] angiotensin II inhibitors,[4b] antifungal,[4c] anti-inflammatory,[4d] anticancer agents[4e,f] and inhibitors of p^{38} MAP kinase,[4g,h] apart from behaving as plant growth regulators.[4i] Substituted imidazoles have also found applications as functional materials in organic electroluminescent devices (OLED),[5a−c] conjugated and functional polymers,[5d] in coordination chemistry as important ligands,[6a] metalloenzymes,[6b,c] and non natural metal complexes[6d] precursors of stable carbene ligands[7a] and as NHCS[7b] and ionic liquids.[8] Therefore, a good deal of interest exists in developing new, efficient, atom economical complementary methods for the synthesis of functionalized tri- and tetrasubstituted imidazoles with absolute regiocontrol.[9,10]

Multicomponent reactions play an important role in organic synthesis and are a powerful tool for generating molecular complexity and diversity with greater efficiency in a one-pot process from readily available precursors.[11] These reactions also form a basis for the synthesis of substituted imidazoles. Thus, 2,4,5-tri- and 1,2,4,5-tetrasubstituted imidazoles are generally synthesized by three or four component cyclocondensation of either 1,2-diketones,[12,13] α-hydroxy-,[13] acetoxy-,[13] silyloxyketones, α-ketomonooximes or nitriles[13e] with aldehydes and ammonium acetate and/or primary amines usually under classical heating or in refluxing acetic acid. However, these reactions, although effective for certain substrates, sometimes give poor yields of imidazoles, requiring longer reaction time,[13] besides, in four component condensation reactions, imidazoles were obtained in varying level of purity after laborious workup and purification. Therefore, many efforts have been made in recent years to improve the reaction conditions[14] by performing these reactions under microwave,[15a−d] ultrasonic,[15e] or under superheating

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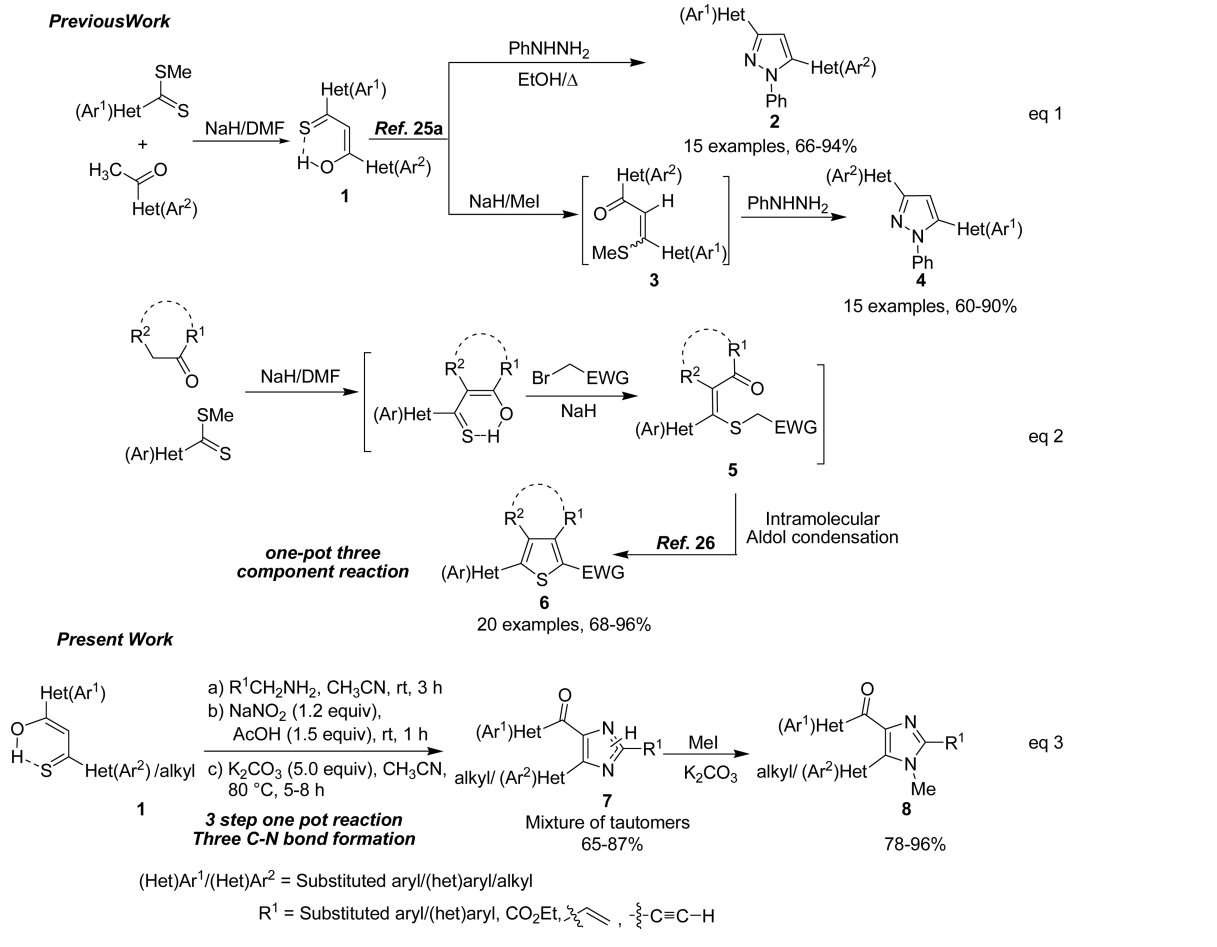
conditions using continuous flow microreactor,[15f] and also in the presence of various Lewis acid catalysts. Thus, a large variety of catalysts such as silica gel/zeolite HY, silica gel/$NaHSO_4$ or $HClO_4$–SiO_2, silica supported sulfuric acid, BF_3·SiO_2 heteropolyacids, $InCl_3$·$3H_2O$, $NiCl_2$·$6H_2O$, Al_2O_3, ceric ammonium nitrate, ionic liquids, molecular iodine or proline have been employed to improve the yields of substituted imidazoles in these reactions.[15g] However, these multicomponent approaches toward substituted imidazoles are usually restricted to a fixed pattern of substitution, mostly 4,5- bishet(aryl)imidazoles, and do not address the regiochemical problem, as most of the precursors are usually symmetrically substituted diaryl/het(aryl)ketones or their analogues furnishing only symmetrically substituted 4,5-diaryl/het(aryl)imidazoles.[15,16] Some of the earlier classical methods for imidazole synthesis[15a] include reaction of α-haloketones with amidines,[16,17] cyclocondensation of α-acylaminoketones with ammonium acetate[18] and base promoted reaction of *p*-tosylmethyl isocyanide with aldimines/imidoyl chloride (van Leusen reaction).[19] In recent years, a range of new synthetic routes[20] including stepwise substitution reactions on simple imidazoles, transition metal catalyzed cyclizations of acyclic precursors[9d,e,21] and organocatalytic methods[22] have been developed.[23] However, many of these reactions are problematic and suffer from one or more limitations such as harsh reaction conditions, unsatisfactory product yield, lack of generality and substituent compability, tedious isolation procedures, expansive and detrimental metal precursors. Therefore, the development of new, efficient and general synthetic routes for multisubstituted imidazoles with absolute regiocontrol from easily accessible starting materials is still of great importance and remains a formidable challenge.

Our own interest in imidazole synthesis derives from our continuous endeavors aimed at devising new synthetic methods for five and six membered heterocycles employing organosulfur building blocks such as polarized ketene dithioacetals, the corresponding N,S-acetals and their newly developed synthetic variants.[24] In this context, we have recently reported the synthesis and applications of unsymmetrically substituted 1,3-bishet(aryl)monothio-1,3-diketones of the general structure **1**, a new class of versatile organosulfur synthons, which are readily available in good yields, by base mediated condensation of active methylene ketones and het(aryl)/alkyl dithioesters.[25a] These 1,3-monothioketones **1** can be considered as 1,3-diketone surrogates displaying significantly different reactivity and electronic properties at carbonyl and thiocarbonyl groups, which could overcome shortcomings associated with 1,3-diketones as 3- carbon 1,3- bielectrophilic precursors for regioselective synthesis of five and six membered heterocycles.[25a] Indeed, in our recent papers, we have addressed this regioselectivity problem and have reported an efficient regiocontrolled synthesis of unsymmetrically substituted 1-aryl-3,5-bishet(aryl)pyrazoles[25a] and 3,5-bishet(aryl)oxazoles[25b] using 1,3-monothioketones **1** as 1,3-bielectrophilic three carbon components and their subsequent transformations (Scheme 1, eq 1). Recently, we had also described a sequential one-pot synthesis of tri- and tetrasubstituted thiophenes **6** and fluorescent push–pull thiophene acrylates

Scheme 1. Synthesis of Heterocycles from 1,3-Bishet(aryl)monthio1,3-diketones 1



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through in situ generated 1,3-monothioketones (Scheme 1, eq 2).[26] In continuation of these studies, directed toward exploring synthetic applications of these 1,3-bishet(aryl)-monothio-1,3-diketones, we now report a regiocontrolled sequential one-pot synthesis of 2-substituted-4(5)-(acyl)-5(4)-het(aryl)/alkylimidazoles **7** and their subsequent alkylation to the corresponding *N*-methyl analogues **8** (Scheme 1, eq 3). The overall strategy involves formation of three C−N bonds in contiguous fashion via (1) regioselective condensation of 1,3-monothioketones with substituted α-methylamines generating enaminones **13**, (2) in situ α-nitrosation of enaminones **13** with sodium nitrite and acetic acid to give the corresponding α-hydroxyiminoimine intermediates **14**, (3) base mediated in situ cyclodehydration of hydroxyiminoimines **14** to imidazoles **7** (see Scheme 3).

RESULTS AND DISCUSSION

Despite several elegant syntheses of substituted imidazoles, reported in the literature, a direct general approach involving cycloannulation of *N*-alkylenaminones/enaminoesters with an electrophilic nitrogen is still lacking (Figure 1).[27] Enaminones

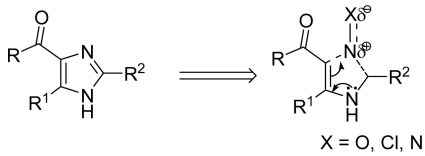


Figure 1. Proposed synthesis of 2,4,5-substituted imidazoles from enaminones.

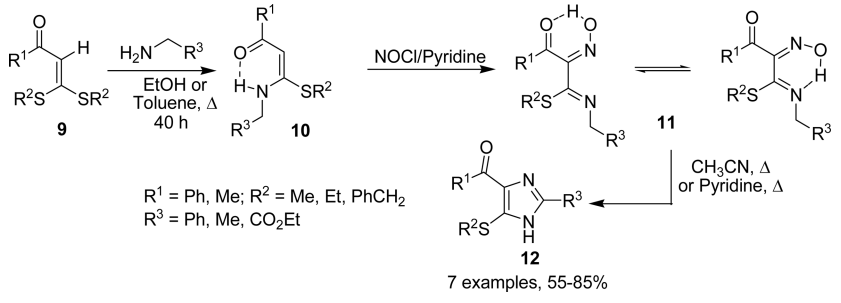
and enaminoesters are shown to be versatile intermediates for heterocycle synthesis.[28] Several years ago, during the course of our investigation on synthetic applications of α-oxoketene N,S-acetals, a class of versatile functionalized enaminones,[24a,29] we had described in a preliminary communication, a novel route to few 4-acyl-5-(alkyllthio)-2-phenylimidazoles **12** through nitrosation of α-oxoketene-S-(alkylthio)-*N*-(benzyl)acetals **10** with nitrosyl chloride in pyridine to the corresponding α-hydroxyiminoimines **11** and their subsequent cyclodehydration in refluxing acetonitrile/pyridine (Scheme 2).[30] This reaction, however, employs toxic nitrosyl chloride gas, as nitrosating agent, along with difficult workup, involving a three step process, starting from displacement reaction on α-oxoketene dithioacetals **8**[29a] with benzylamine under prolonged heating in ethanol or toluene[29a,b,31] to furnish the corresponding N,S-acetals **10** in only moderate to good yields.

Besides, the scope and generality of this reaction was not further examined, which was limited only to few 2-phenyl(one example of 2-carboethoxy)-4-aroyl-5-(alkylthio)-imidazoles **12** (Scheme 2). We therefore conceived of developing a milder, more efficient, one-pot version of this protocol with broader substituent scope for the synthesis of 2,4,5-trisubstituted imidazoles such as **7**, by employing unsymmetrically substituted 1,3-bishet(aryl)/alkyl monothioketones **1** as precursors for enaminones **13** and sodium nitrite as nitrosating agent as depicted in the Scheme 1 (eq 3) and Scheme 3.

We first examined the stepwise conversion of 1,3-monothioketones **1** to imidazoles **7** (via enaminone **13** and hydroxyiminoimines **14**) and selected monothio-1,3-diketone **1a** and benzylamine as model substrates for optimization of reaction conditions (Scheme 3). Thus, **1a** reacted with benzylamine efficiently at room temperature in various solvents like acetonitrile, ethanol or DMF, in highly regiocontrolled fashion, affording the corresponding *N*-benzylenaminone **13a** in excellent yields within 3 h (Scheme 3). Nitrosation of enaminone **13a** was next examined with milder nitrosating agents such as sodium nitrite/acetic acid or isoamyl nitrite in the presence of various solvents, with a view to synthesize α-hydroxyiminoimine intermediate **14a**. Thus, best results were obtained, when enaminone **13a** was reacted with sodium nitrite and acetic acid (1.5 equiv) in acetonitrile as solvent at room temperature, furnishing the hydroxyiminoimine **14a** in 85% yield within 1 h (Scheme 3, Table S1, Supporting Information). The nitrosoenaminone **14a**, thus obtained, was subjected to intramolecular cyclodehydration to imidazole **7a** by heating in various solvents like pyridine, toluene, DMSO, DMF and acetonitrile under neutral conditions, as well as, in the presence of mild base like potassium carbonate (Table S2, Supporting Information). The imidazole **7a** was formed in all these conditions in good yields, whereas best yield (87%) of **7a** was obtained by cyclization of **14a** in refluxing acetonitrile in the presence of potassium carbonate as base (Scheme 3). The imidazole **7a** was found to exist in two tautomeric form **7aA** and **7aB** at room temperature, however, methylation of **7a** with methyl iodide in the presence of potassium carbonate yielded only single regioisomer, which was characterized as 1-*N*-methyl-2-phenyl-4-benzoyl-5-(4-methoxyphenyl)-imidazole **8a** (Table 1, entry 1) on the basis of its spectral and analytical data as well as by single crystal X-ray analysis (Figure S1, Supporting Information).

Having established the optimized reaction conditions for three step transformation of 1,3-monothioketone **1a** to imidazole **7a** (Scheme 3), we next considered to develop a sequential one-pot synthesis of imidazole **7a** from **1a** and benzylamine. Optimization of the reaction conditions revealed that the imidazole **7a** was obtained in lower yields (61−68%) when isoamylnitrite was employed as nitrosating agent in various solvents under one-pot conditions. However, after considerable experimentation, **7a** could be obtained in optimal yield of 75% in a one-pot operation, by generating the enaminone **13a** from **1a** in acetonitrile as solvent, and by employing sodium nitrite/acetic acid as nitrosating

Scheme 2. Synthesis of 2,4-Substituted-5-(alkylthio)imidazoles from α-Oxoketene-N,S-acetal



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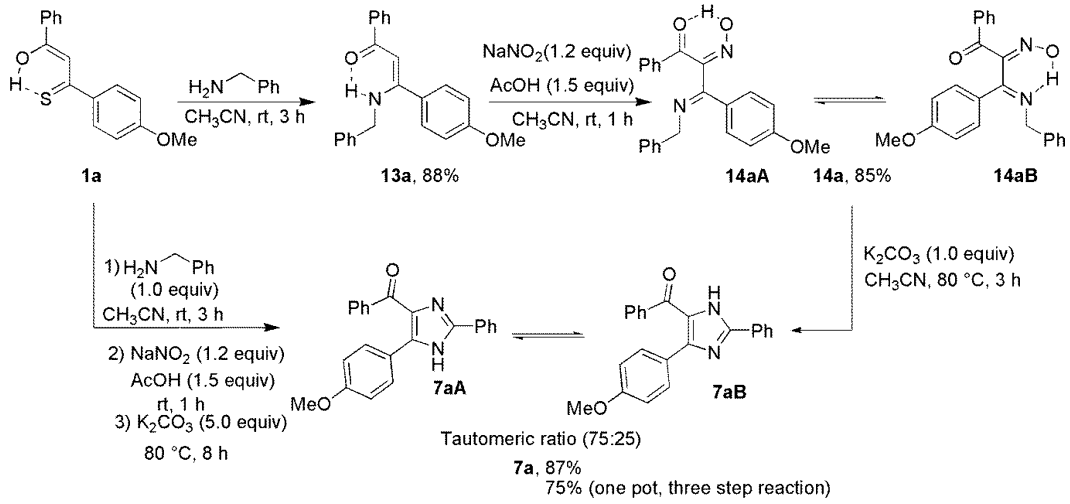
Scheme 3. Synthesis of Imidazole 7a from 1,3-Bis(aryl)monthio1,3-diketone 1a



agent (in acetonitrile), followed by heating the reaction mixture in the presence of excess (5 equiv) of potassium carbonate (Table S3, Supporting Information). Despite lower yield (75%) of imidazole **7a** compared to stepwise process, these optimized one-pot conditions were used throughout our studies for the synthesis of various 2,4,5-trisubstituted imidazoles **7** (Table 1, entries 2−12), (Table 2, entries 1−3), (Scheme 4).

With the optimized reaction conditions in hand for one-pot synthesis of imidazole**7a** from 1,3-monothiodiketone **1a** (Scheme 3, Table 1, entry 1), we next evaluated the generality and scope of this reaction with respect to various substituents at 2-, and 4(5)- positions of imidazole framework. These results are displayed in Table 1. Thus, by employing a range of unsymmetrically substituted het(aryl)-1,3-monothioketones **1** and various α-het(aryl)methylamines, it was possible to install a variety of substituted aryl- and het(aryl)- (2-thienyl-, 2-furyl-, 2-(*N*-methyl)pyrrolyl-) groups at 2- and 4(5)- positions of imidazoles **7** (entries 2−5). Entries 3−4 also represent examples of introduction of sterically congested (2-methoxyphenyl) group at either 2- or 4(5) position of imidazole ring. Similary, the imidazoles **7f** and **7g** carrying an alkyl (*n*-butyl-) or acetyl group respectively at 4(5) positions could also be obtained in good yields from the corresponding 1-(*n*-butyl)-3-aryl 1,3-monothiodiketone **1e** or α- (thioaroyl)acetone **1f** under identical conditions (Table 1, entries 6 and 7). This new one-pot protocol was found to be equally efficient for the introduction of functionalities such alkoxycarbonyl or a vinyl group at 2- position of imidazoles by utilizing either ethyl glycinate or allylamine as annulating partners, thus affording the corresponding 4(5)-substituted imidazole- 2-carboxylates **7h−i** (entries 8−9) and 2-vinylimidazoles **7j−k** (entries 10−11) respectively in good yields. The corresponding α-oxoketene-N,S-acetal **10a** also underwent one-pot nitrosation and intramolecular cyclization in the presence of potassium carbonate in refluxing acetonitrile or pyridine (61%) to afford the corresponding 4(5)-(methylthio)imidazole **12a** in good yields as single tautomer (Table 1, entry 12).[30a] However, the attempted synthesis of the corresponding 2-methylimidazole **7l** from either 1,3-monothioketone **1g** and ethylamine (under one-pot condition) or from *N*-ethylhydroxyiminoimine **14l** by treatment with potassium carbonate under previous conditions, did not meet with any success, yielding only intractable reaction mixture (Table 1, entries 13−14).

The present methodology was also extended for the synthesis of 4(5)-(2-hydroxyphenyl) substituted imidazoles such as **7m−o**, which are known to act as good coordinating ligands for various metal ions (Table 2).[32] Thus, the 1,3-monothioketones **1j−l** bearing a [2-(4-methoxybenzyloxy)phenyl] group at thiocarbonyl moiety were subjected to sequential amination with various het(aryl)amines followed by nitrosation and intramolecular cyclocondensation under earlier described one-pot conditions, to afford the corresponding 4(5)-[2-(4-methoxybenzyloxy)phenyl] substituted imidazoles **7m′−o′** in good yields (Table 2, entries 1−3). Subsequent deprotection of (4-methoxybenzyloxy) group in **7m′−o′** with TFA, furnished the corresponding 4(5)-(2-hydroxyphenyl)-5(4)-het(aroyl)imidazoles **7m−o** in high yields (Table 2, entries 1−3). Alternatively, alkylation of imidazoles **7m′−o′** with methyl iodide under previously described conditions, followed by TFA mediated deprotection of (4-methoxybenzyloxy) group in crude *N*-methylimidazoles **8m′−o′**(without isolation), afforded the corresponding 1-(*N*-methyl)-5-(2-hydroxyphenyl)-2-het(aryl)-4-het(aroyl)imidazoles **8m−o** in good yields (Table 2, entries 1−3).

We also elaborated this method for the synthesis of 2-ethynylimidazoles such as **7p**, by reacting 1,3-monothioketone **1m**, sequentially with propargylamine, sodium nitrite and potassium carbonate under previously described one-pot conditions, providing **7p** in moderate yield (54%), which could be improved to 76%, when pure *N*-propargylhydroxyiminoimine **14p** was subjected to cyclodehydration in the presence of potassium carbonate (Scheme 4). However, the generality of this reaction for the synthesis of 2-ethynylimidazoles could not be established, and attempted intramolecular cyclization of *N*-propargylhydroxyiminoimine **14q** in the presence of K_2CO_3 did not give the expected imidazole **7q**, but a different product, which could not be characterized. Interestingly, attempted intramolecular thermal cyclodehydration of hydroxyiminoimine **14p** to imidazole **7p** in DMSO at 100 °C gave a new product (59%), which was characterized as the 2,3-substituted pyridine **15a** on the basis of its spectral and analytical data (Scheme 4). Similarly the hydroxyiminoimine **14q** also furnished the 2,3-disubstituted pyridine **15b** in 65% yield under identical conditions. Our search of literature revealed that such kind of substituted pyridines have been reported to be formed by intramolecular cyclization of *N*-propargylenaminones in the presence of copper(I) salt.[28h] We therefore subjected the

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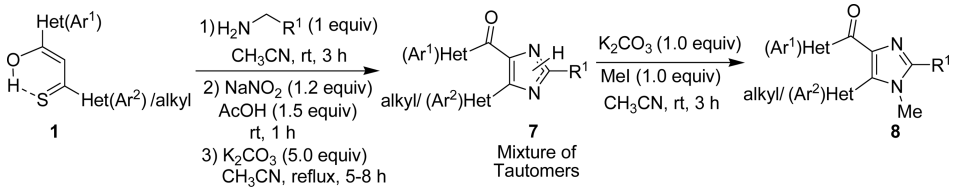
Table 1. Synthesis of 2,4,5-Tri- and 1,2,4,5-Tetrasubstituted Imidazoles 7 and 8



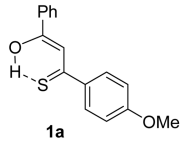
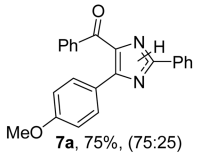
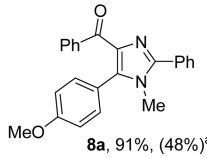
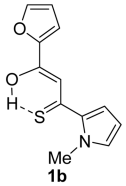
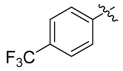
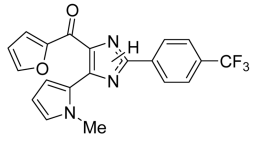
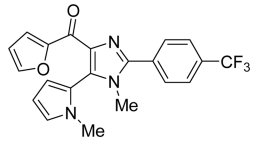
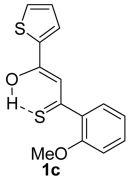
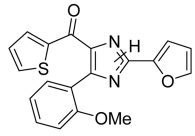
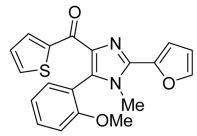
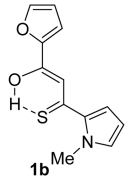
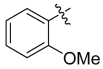
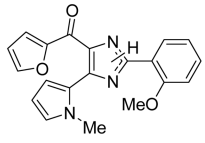
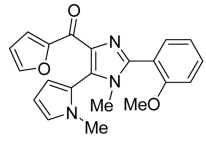
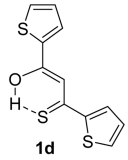
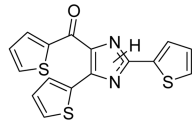
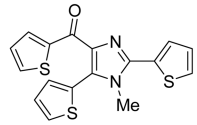
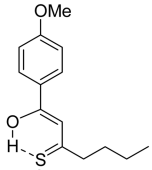
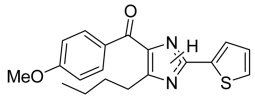
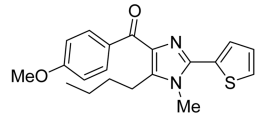
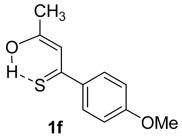
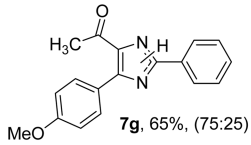
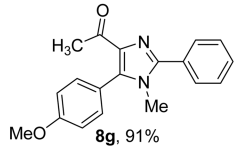
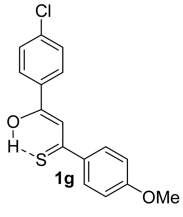
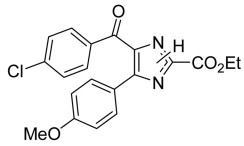
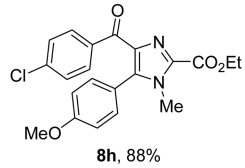
entry	1	H_2N R^1	7 % yield, (tautomeric ratio)	8 % yield
1	 **1a**		 **7a**, 75%, (75:25)	 **8a**, 91%, (48%)[a]
2	 **1b**		 **7b**, 87%, (50:50)	 **8b**, 93%
3	 **1c**		 **7c**, 82%, (100:0)	 **8c**, 90%
4	 **1b**		 **7d**, 81%, (55:45)	 **8d**, 96%
5	 **1d**		 **7e**, 71%, (100:0)	 **8e**, 89%
6	 **1e**		 **7f**, 67%, (90:10)	 **8f**, 84%
7	 **1f**		 **7g**, 65%, (75:25)	 **8g**, 91%
8	 **1g**		 **7h**, 68%, (75:25)	 **8h**, 88%

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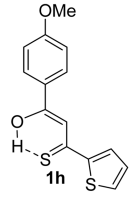
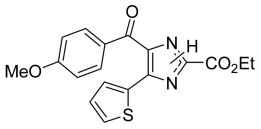
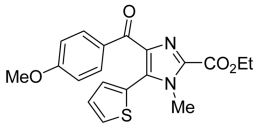
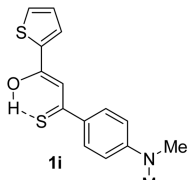
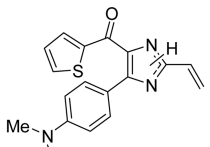
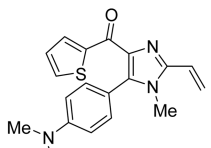
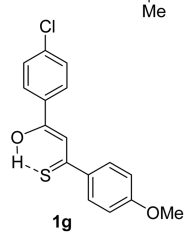
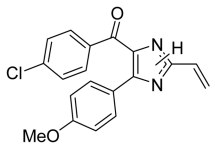
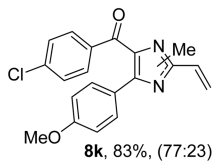
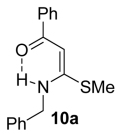
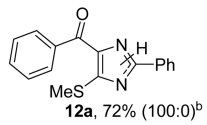
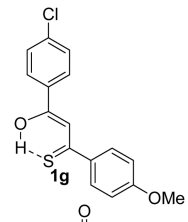
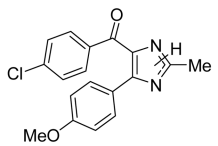
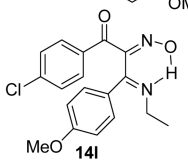
Table 1. continued

entry	1	H_2N R^1 R^1	7 % yield, (tautomeric ratio)	8 % yield
9			 **7i**, 71%, (100:0)	 **8i**, 89%
10			 **7j**, 71%, (100:0)	 **8j**, 88%
11			 **7k**, 81%, (80:20)	 **8k**, 83%, (77:23)
12			 **12a**, 72% (100:0)[b]	–
13			 **7l**, 0%	–
14[c]			**7l**, 0%	–

[a]Yield obtained under one-pot condition. [b]Obtained by one-pot nitrosation of N,S-acetal and intramolecular cyclization in the presence of K_2CO_3 (5.0 equiv) and CH_3CN. [c]K_2CO_3 (1.0 equiv), CH_3CN, 80 °C, 5−12 h.

enaminones **13p−q** to thermal intramolecular cyclization in DMSO, which also afforded the pyridines **15a−b** in comparable yields (Scheme 5).

Prototopic Tautomerism of *NH* Imidazoles 7. Most of the newly synthesized 4(5)- unsymmetrically substituted *NH* imidazoles **7a−k** and **7m−p** (Tables 1, 2 and Scheme 4) display prototropic annular tautomerism[33] as evident from their ^{1}H NMR spectra. Depending on the nature of substituent on either 4- or 5- positions, one tautomer may predominate over the other (Table 1).[34] However, alkylation of these imidazoles with methyl iodide in the presence of potassium carbonate, afforded only single regioisomers, i.e., 1-*N*-methyl-2,5-bis het(aryl)-4-het(aroyl)imidazoles **8a−j** and **8m−o** in highly regiocontrolled fashion (Table 1, entries 1−10 and Table 2, entries 1−3), with only few exceptions, wherein a mixture of regioisomeric 1/3-*N*-methylimidazoles were obtained (Table 1, entry 11 and Scheme 4). The regiochemistry of these *N*-methylimidazoles **8** was further confirmed by single crystal X-ray analysis of imidazole **8a** as well as that of sterically crowded derivative **8d** (Table 1, entries 1 and 4), (Figure S1 and S2, Supporting Information). The regioselective formation of only *N*-methylimidazole **8** from **7** could be rationalized in terms of formation of a more stabilized anion on nitrogen (**7A**) due to its delocalization over carbonyl group (Figure 2).

Although we have not carried out a detailed study of prototopic tautomerism of nitrosoenaminone **14a**, however, a comparison of ^{1}H NMR spectra of both enaminone **13a** (Figure S48, Supporting Information) and **14a** (Figure S51, Supporting Information) ruled out nitrosoenaminone structure **14aC** or **14aD** (Figure 3). Thus, signal due to *NH* proton in the enaminone **13a**, both in $CDCl_3$ and DMSO-d_6, appears around δ11.6−11.7 as broad triplet (J = 6.0 Hz), whereas benzylic methylene protons are present as sharp doublet (J = 6.0 Hz) at δ 4.4 due to the vicinal coupling between $-NHCH_2-$ protons, thus supporting the intramolecular

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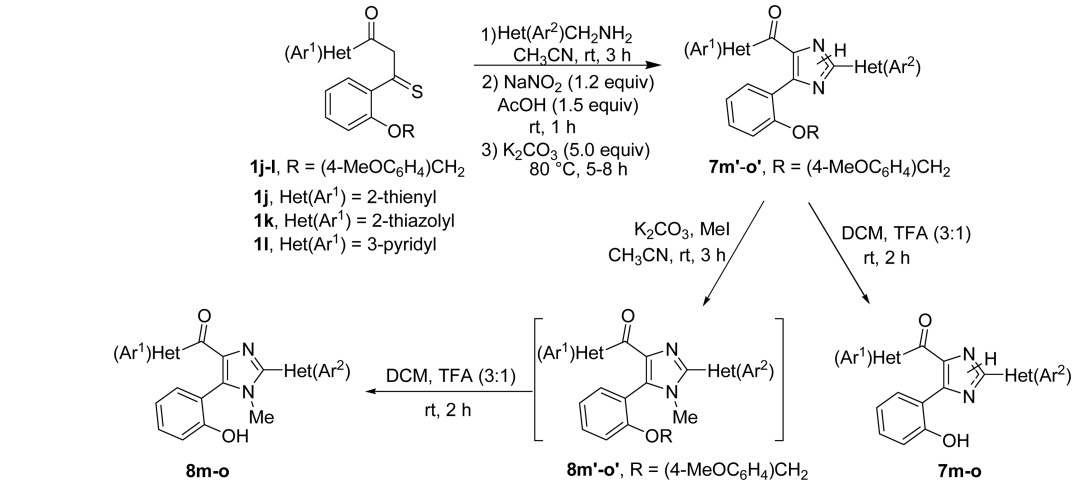
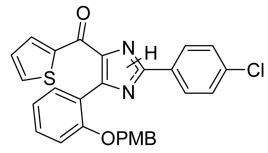
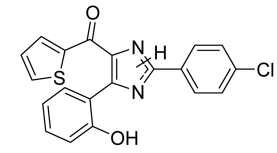
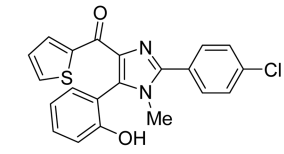
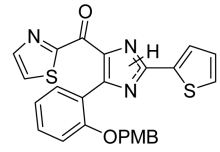
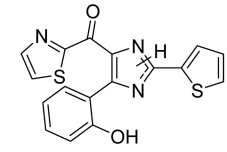
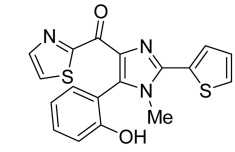
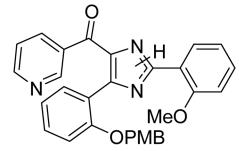
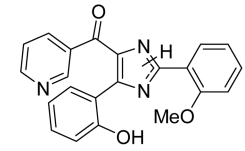
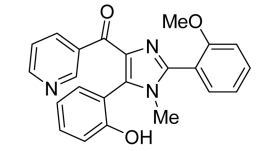
Table 2. Synthesis of 2-Het(aryl)-4(5)-het(aroyl)-5(4)-(2-hydroxyphenyl)imidazoles



entry	7' % yield, (tautomeric ratio)	7 % yield, (tautomeric ratio)	8 % yield
1	 **7m'**, 82% (100:0)	 **7m**, 85% (50:50)	 **8m**, 78%
2	 **7n'**, 85% (75:25)	 **7n**, 80% (75:25)	 **8n**, 89%
3	 **7o'**, 77% (90:10)	 **7o**, 80% (100:0)	 **8o**, 82%

H- bonded enaminone structure **13a** (Scheme 3). On the other hand, in the ^{1}H NMR spectrum of nitrosoenaminone **14a** in DMSO-d_6, the lower field labile proton appears as a sharp singlet at δ 13.1, whereas the benzylic methylene protons are present as AB quartet displaying geminal coupling of the order of 16.0 Hz (Figure S16, Supporting Information). The absence of coupling between benzylic CH_2 and low field labile proton rules out the nitrosoenaminone structures **14aC** or **14aD**, and points to the intramolecularly H-bonded hydroxyiminoimine tautomeric structures such as **14aA**−**14aB** (Figure 3). The appearance of methylene protons as AB quartet in the ^{1}H NMR spectrum of **14a**, is probably due to restricted rotation around CH_2−N bond in the hydrogen bonded structure **14aB** (Figure 3). However, further study is required to confirm these structures. The ^{1}H NMR spectra of both *N*-propargyl enaminone **13p** and the corresponding nitroso analogue **14p** also displayed similar features.

Mechanism of the Formation of Imidazoles 7 from Hydroxyiminoimines 14. As we have observed earlier (Table S2, Supporting Information), the hydroxyiminoimine intermediate **14a** undergoes intramolecular thermal cyclodehydration to imidazole **7a** in varying yields in solvents like DMSO, toluene, DMF or acetonitrile under prolonged heating. On the other hand, in the presence of weaker base like K_2CO_3, in refluxing acetonitrile, the reaction proceeds smoothly within 7−8 h, yielding imidazole **7a** in 87% yield (Table S2, Supporting Information). We therefore propose two possible mechanisms for the formation of imidazoles **7** from α-hydroxyiminoimines **14** as shown in the Scheme 5. Thus, under basic conditions, the hydroxyiminoimine **14** undergoes proton abstraction to oximate anion **16A**, which exists in equilibrium with carbanionic species **16B**. The intermediate **16B** undergoes facile electrocyclization and elimination of OH group, through delocalized anion **16C** affording imidazole **7** through tautomeric intermediate **17**. Failure to obtain 2-methylimidazole **7l** from hydroxyiminoimine **14l** (Table 1, entries 13−14) is probably due to lower acidity of aminomethylene protons in **14l**, thus resisting the abstraction of

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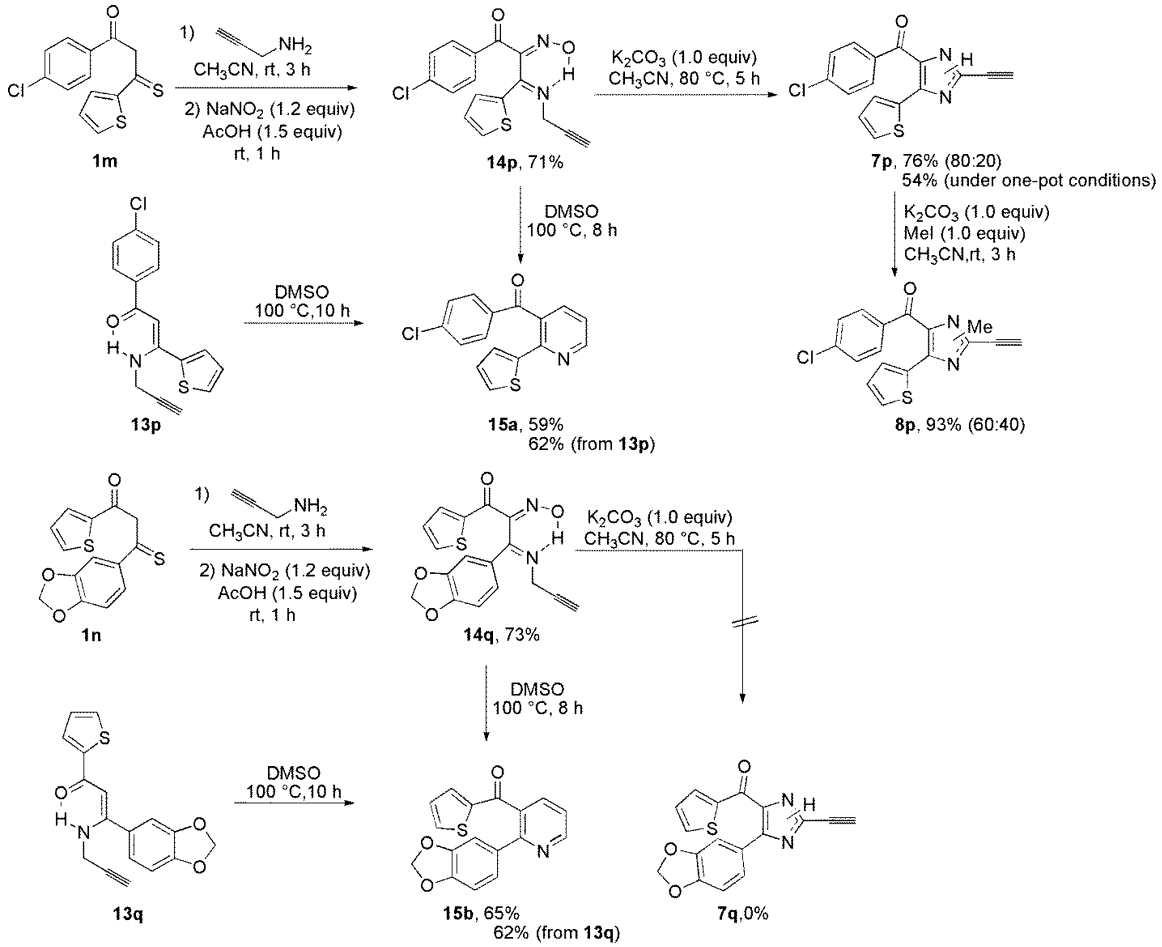
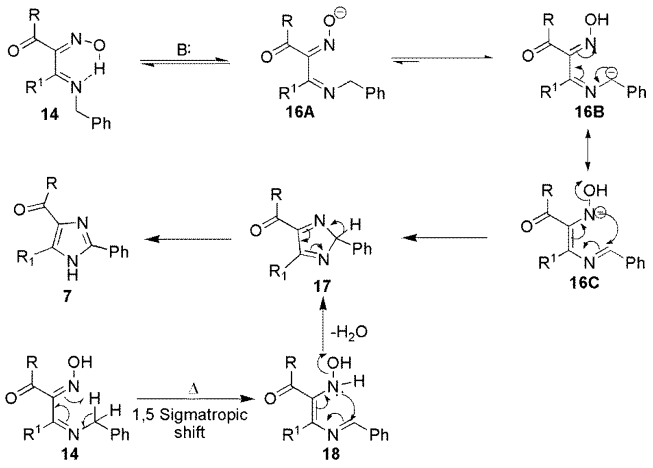
Scheme 4. Synthesis of 2-Ethynyl-4,5-Substituted Imidazole and 2,3-Disubstituted Pyridines



Scheme 5. Probable Mechanism of Formation of Imidazoles 7 from Hydroxyiminoimines 14



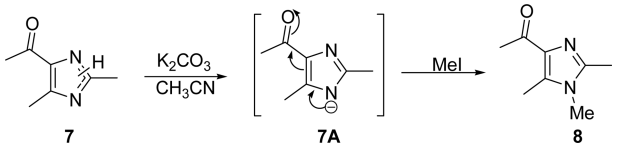


Figure 2. Regioselective *N*-methylation of imidazoles **7** to 1-*N*-methyl-4-het(aroyl)-2,5-substituted imidazoles **8**.

proton by weaker base like potassium carbonate and formation of the corresponding carbanion for electrocyclization to imidazole **7l**. On the other hand, under neutral thermal conditions, the intermediate **17** appears to be formed via a 1,5-prototopic shift in the hydroxyiminoimine **14** and subsequent intramolecular dehydrative cyclization of the resulting imine intermediate **18** (Scheme 5).

Mechanism of the Formation of Pyridines 15a–b from Enaminones 13p–q and Hydroxyiminoimines 14p–q. Cacchi and co-workers have reported synthesis of substituted pyridines via CuBr (0.4 equiv) catalyzed intramolecular cyclization of *N*-propargylenaminones such as **13** in DMSO.[28h] They have proposed a mechanism involving complexation of Cu^{+} species to triple bond, which facilitates 6-*endo*-cyclization to pyridines **15** by intramolecular nucleophilic attack of enaminone (α- to the carbonyl group) on acetylenic terminal carbon atom. On the other hand, we have observed the formation of pyridines **15a–b** in comparable yields, from either enaminones **13p–q** or the corresponding hydroxyiminoimine analogues **14p–q** on heating in DMSO in the absence of copper catalyst (Scheme 4). We therefore propose a different mechanism for the formation of pyridines **15a–b** as shown in the Scheme 6. Thus, the enaminones **13** or **14** undergo two consecutive thermal 1,3- prototopic shifts to afford the azatriene intermediate **20** (through allene intermediate **19**). Subsequent electrocyclization of azatriene **20** to dihydropyridine **21** followed by its dehydrogenation (X = H) or dehydrogenative elimination of nitric oxide (X = NO) furnishes the pyridines **15a–b** in good yields (Scheme 6).

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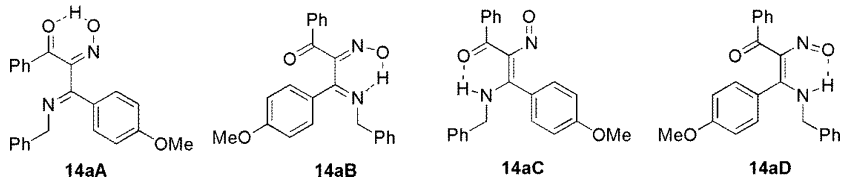
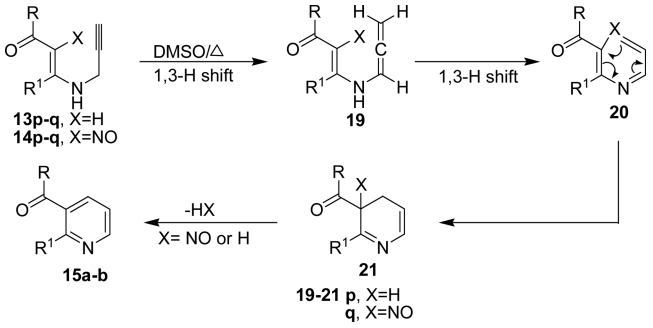


Figure 3. Prototropic tautomers of **14a**.

Scheme 6. Probable Mechanism for the Formation of Pyridines 15 from Enaminones 13p−q and 14p−q



CONCLUSION

In summary, we have developed an efficient, highly regiocontrolled, one-pot [2 + 2 + 1] annulation approach for the synthesis of a series of diversely functionalized trisubstituted 4(5)-het(aroyl)-2,5(4)-het(aryl)/alkylimidazoles, from readily available precursors, i.e., 1,3-bishet(aryl)monothio-1,3-diketones, α-substituted methylamines and sodium nitrite (as precursor for ring nitrogen) and their subsequent alkylation to the corresponding *N*-methyl derivatives. This novel sequential one-pot protocol, wherein three new carbon nitrogen bonds are formed in contiguous fashion, involves in situ generation of enaminones from monothio-1,3-diketones, followed by their α-nitrosation to α-hydroxyiminoimines and subsequent base mediated intramolecular heterocyclization of α-hydroxyiminoimines to imidazoles in high yields under mild conditions. Also, by appropriate choice of the 1,3-monothiodiketones and substituted aminomethylene partners, it is possible to modulate a large variety of substituents at 2,4,5-positions of final imidazole products. The method provides rapid access, especially to imidazoles with sterically demanding (het)aromatic groups on 2 and (4)5- positions, as well as to 4(5)- (2-hydroxyphenyl) imidazoles, which are known to be good coordinating ligands. It should be noted that several synthesis of substituted imidazoles with het(aryl) substituents at 2,4,5 positions have been reported in the literature, whereas the direct general convergent methods for the synthesis of 4(5)-acyl substituted imidazoles are only few in the literature.[20a,c,21c,23a] Also noteworthy is the ease with which 1,3-monothiodiketones react with α-substituted methylamines to give enaminoketones under very mild conditions in highly regiocontrolled fashion, since the reported synthesis of enaminoketones[28a,b] from unsymmetrically substituted 1,3-diketones[28a,b] require drastic conditions and is not regioselective.[35] Although the present methodology is limited only to the synthesis of 4(5)-het(aroyl)-substituted imidazoles, further work to extend the scope of the reaction for the introduction of other functionalities in the imidazole ring, such as carboalkoxy/cyano groups via *N*-benzylenaminoesters and *N*-benzylenaminonitriles respectively, or by further transformations of het(aroyl) group (i.e., cleavage of ketone by Baeyer-Villiger reaction) are in progress.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial suppliers and used without further purification. Solvents were dried according to the standard procedures. All the reactions were monitored by thin layer chromatography using standard TLC silica gel plates and visualized with UV light. Column chromatography was performed using silica gel (100−200 mesh). Nuclear magnetic resonance spectra were recorded on (400 MHz) FT-NMR spectrometer with $CDCl_3$ or DMSO-d_6 as solvent. Chemical shifts were reported in δ ppm using residual solvent protons as internal standard (δ 7.26 for $CDCl_3$ and δ 2.50 for DMSO-d_6 in ^{1}H NMR, δ 77.16 for $CDCl_3$ and δ 39.52 for DMSO-d_6 in ^{13}C NMR). Coupling constants were reported as *J* values in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sex (sextet), dd (double doublet), dt (doublet of triplet), td (triplet of doublet), ddd (doublet of doublet of doublet), m (multiplet) and br (broad). Infrared spectra of neat samples were recorded in ATR (attenuated total reflectance) mode using FT-IR instrument and HRMS on Q-TOF spectrometer. Melting points were recorded using an electrothermal capillary melting point apparatus and are uncorrected.

General Procedure for the Synthesis of 1,3-Bishet(aryl)-monothio-1,3-diketones 1a−n. The desired 1,3-bishet(aryl)-monothio-1,3-diketones were prepared following our earlier reported procedure.[25a] To a stirred suspension of NaH (240.0 mg, 10.0 mmol, 60% suspension in mineral oil) in dry DMF (10 mL) under N_2 atmosphere, a solution of het(aryl) methyl ketone (5.0 mmol) and het(aryl) dithioester (5.0 mmol) in DMF (10 mL) was added dropwise at 0 °C and the reaction mixture was stirred at room temperature for 1h (monitored by TLC). It was then poured into ice-cold water (100 mL), acidified with acetic acid (1 mL), extracted with EtOAc (3 × 50 mL), the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

The known 1,3-bishet(aryl)-monothio-1,3-diketones **1a−b**,[25b] were characterized by comparison of their spectral and analytical data with literature data. The spectral and analytical data of unknown 1,3-bishet(aryl)-monothio-1,3-diketones **1d**, **1f−i** and **1j−n** are given below. The monothio-1,3-diketones **1c** and **1e** were found to be unstable during purification by column chromatography and used as such for the preparation of imidazoles **7c** and **7f** without purification.

*(Z)-3-Hydroxy-1,3-di(thiophen-2-yl)prop-2-ene-1-thione (**1d**).* Obtained as a red solid (970.2 mg, 77%): mp 65−67 °C; R_f 0.3 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2998, 1569, 1402, 1242, 702; ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.66 (s, 1H), 7.86 (d, *J* = 3.6 Hz, 1H), 7.75 (d, *J* = 4.0 Hz, 1H), 7.65 (d, *J* = 5.2 Hz, 1H), 7.62 (d, *J* = 5.2 Hz, 1H), 7.34 (s, 1H), 7.18 (t, *J* = 4.0 Hz, 1H), 7.15 (t, *J* = 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.6, 171.7, 151.6, 140.1, 133.7, 132.3, 130.3, 128.81, 128.79, 127.6, 106.7; HRMS (ESI) *m*/*z* calcd for $C_{11}H_9OS_3$ $[M + H]^+$ 252.9816, found 252.9808.

*(Z)-3-Hydroxy-1-(4-methoxyphenyl)but-2-ene-1-thione (**1f**).* Obtained as a red solid (676.0 mg, 68%): mp 55−57 °C; R_f 0.5 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 2925, 1583, 1553, 1446, 1239, 784; ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.93 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.74 (s, 1H), 3.86 (s, 3H), 2.23 (s, 3H);

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$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.7, 186.0, 162.7, 137.1, 128.9, 113.8, 112.1, 55.6, 26.1; HRMS (ESI) m/z calcd for $C_{11}H_{13}O_2S$ $[M + H]^+$ 209.0636, found 209.0626.

*(Z)-3-(4-Chlorophenyl)-3-hydroxy-1-(4-methoxyphenyl)prop-2-ene-1-thione (**1g**).* Obtained as a red solid (1.15 g, 76%): mp 95−97 °C; R_f 0.4 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2834,1585, 1435, 1261, 791; ^1H NMR (400 MHz, $CDCl_3$) δ 15.77 (s, 1H), 7.92 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.8 Hz, 2H), 7.38 (s, 1H), 6.93 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 206.0, 176.9, 162.9, 138.7, 138.3, 134.3, 129.3, 129.0, 128.5, 114.0, 108.6, 55.7; HRMS (ESI) m/z calcd for $C_{16}H_{14}ClO_2S$ $[M + H]^+$ 305.0403 and 307.0374, found 305.0401 and 307.0372.

*(Z)-3-Hydroxy-3-(4-methoxyphenyl)-1-(thiophen-2-yl)prop-2-ene-1-thione (**1h**).* Obtained as a red solid (993.6 mg, 72%): mp 78−80 °C; R_f 0.4 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2892, 1557, 1397, 1214, 744; ^1H NMR (400 MHz, $CDCl_3$) δ 16.24 (s, 1H), 7.96 (d, J = 9.2 Hz, 2H), 7.76 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 7.60 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.42 (s, 1H), 7.13 (dd, J = 5.2 Hz, 4.0 Hz, 1H), 6.98 (d, J = 9.2 Hz, 2H), 3.89 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.5, 176.5, 163.6, 152.5, 133.7, 129.2, 128.7, 127.4, 127.0, 114.5, 106.3, 55.7; HRMS (ESI) m/z calcd for $C_{14}H_{13}O_2S_2$ $[M + H]^+$ 277.0357, found 277.0350.

*(Z)-1-(4-(Dimethylamino)phenyl)-3-hydroxy-3-(thiophen-2-yl)-prop-2-ene-1-thione (**1i**).* Obtained as a brown solid (1.28 g, 89%): mp 115−117 °C; R_f 0.3 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2921, 1557, 1456, 1249, 790; ^1H NMR (400 MHz, $CDCl_3$) δ 15.70 (s, 1H), 7.93 (d, J = 9.2 Hz, 2H), 7.82 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.58 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.31 (s, 1H), 7.15 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 6.67 (d, J = 9.2 Hz, 2H), 3.07 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 201.2, 171.5, 153.2, 141.6, 132.5, 131.3, 129.4, 129.2, 128.5, 111.1, 106.4, 40.3; HRMS (ESI) m/z calcd for $C_{15}H_{16}NOS_2$ $[M + H]^+$ 290.0673, found 290.0669.

*(Z)-1-(2-(4-Methoxybenzyloxy)phenyl)-3-hydroxy-3-(thiophen-2-yl)prop-2-ene-1-thione (**1j**).* Obtained as a red solid (1.52 g, 80%): mp 55−57 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3070, 1607, 1512, 1233, 761; ^1H NMR (400 MHz, $CDCl_3$) δ 11.58 (s, 1H), 7.59−7.56 (m, 2H), 7.49 (dd, J = 3.6 Hz, 0.8 Hz, 1H), 7.41−7.33 (m, 4H), 7.06−7.02 (m, 3H), 6.82 (d, J = 8.8 Hz, 2H), 5.07 (s, 2H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 180.2, 177.6, 159.6, 154.7, 143.6, 133.8, 132.8, 131.3, 130.60, 130.57, 129.2, 128.7, 128.4, 121.3, 115.9, 114.1, 113.6, 70.7, 55.4; HRMS (ESI) m/z calcd for $C_{21}H_{19}O_3S_2$ $[M + H]^+$ 383.0776, found 383.0773.

*(Z)-1-(2-(4-Methoxybenzyloxy)phenyl)-3-hydroxy-3-(thiazol-2-yl)prop-2-ene-1-thione (**1k**).* Obtained as a brown semisolid (1.58 g, 83%): R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2832, 1583, 1485, 1261, 791; ^1H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.98 (d, J = 3.2 Hz, 1H), 7.84 (s, 1H), 7.65 (d, J = 3.2 Hz, 1H), 7.47 (dd, J = 7.2 Hz, 1.6 Hz, 1H), 7.38−7.33 (m, 3H), 7.03−7.00 (m, 2H), 6.80 (d, J = 8.8 Hz, 2H), 5.08 (s, 2H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 177.1, 176.8, 168.1, 159.4, 154.7, 144.8, 133.4, 131.4, 130.1, 129.1, 128.7, 125.5, 121.1, 115.8, 114.0, 113.5, 70.6, 55.4; HRMS (ESI) m/z calcd for $C_{20}H_{17}NO_3S_2Na$ $[M + Na]^+$ 406.0548, found 406.0542.

*(Z)-1-(2-(4-Methoxybenzyloxy)phenyl)-3-hydroxy-3-(pyridin-3-yl)prop-2-ene-1-thione (**1l**).* Obtained as a red solid (1.60 g, 85%): mp 76−78 °C; R_f 0.3 (3:2 EtOAc/hexane); IR (neat, cm^{-1}) 2921, 1583, 1488, 1239, 784; ^1H NMR (400 MHz, $CDCl_3$) δ 13.29 (s, 1H), 9.01 (d, J = 1.6 Hz, 1H), 8.70 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 7.93 (dt, J = 4.0 Hz, 2.0 Hz, 1H), 7.62 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.46 (s, 1H), 7.40 (td, J = 8.0 Hz, 2.0 Hz, 1H), 7.33−7.28 (m, 3H), 7.06−7.03 (m, 2H), 6.81 (d, J = 8.8 Hz, 2H), 5.06 (s, 2H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1, 178.1, 159.7, 154.2, 152.5, 148.7, 135.2, 134.6, 132.3, 131.9, 131.0, 129.4, 128.4, 123.5, 121.4, 115.0, 114.2, 113.3, 70.8, 55.4; HRMS (ESI) m/z calcd for $C_{22}H_{20}NO_3S$ $[M + H]^+$ 378.1164, found 378.1154.

*(Z)-3-(4-Chlorophenyl)-3-hydroxy-1-(thiophen-2-yl)prop-2-ene-1-thione (**1m**).* Obtained as a red solid (1.21 g, 80%): mp 110−112 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3076, 1581, 1404, 1233, 1053, 704; ^1H NMR (400 MHz, $CDCl_3$) δ 16.02 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 4.4 Hz, 1H), 7.65 (d, J = 4.8 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.39 (s, 1H), 7.16 (t, J = 4.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.8, 174.8, 152.5, 138.8, 134.5, 133.6, 129.4, 128.9, 128.3, 127.9, 106.6; HRMS (ESI) m/z calcd for $C_{13}H_{10}ClOS_2$ $[M + H]^+$ 280.9862 and 282.9832, found 280.9852 and 282.9820.

*(Z)-1-(Benzo[d][1,3]dioxol-5-yl)-3-hydroxy-3-(thiophen-2-yl)prop-2-ene-1-thione (**1n**).* Obtained as a red solid (1.14 g, 79%): mp 65−67 °C; R_f 0.3 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2903, 1557, 1446, 1242, 794; ^1H NMR (400 MHz, $CDCl_3$) δ 14.48 (s, 1H), 7.85 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 7.65 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.40 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.35 (d, J = 2.0 Hz, 1H), 7.25 (s, 1H), 7.17 (dd, J = 5.2 Hz, 4.0 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H), 6.05 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.8, 174.9, 150.6, 148.2, 141.9, 139.0, 132.7, 130.5, 128.7, 122.0, 109.7, 108.2, 107.7, 102.0; HRMS (ESI) m/z calcd for $C_{14}H_{11}O_3S_2$ $[M + H]^+$ 291.015, found 291.0148.

General Procedure for the Synthesis of *N*-Benzyl/propargylenaminones 13a, 13p and 13q. To a stirred solution of 1,3-monothiodiketone (**1a**, **1m**, **1n**) (2.0 mmol) in dry acetonitrile (5 mL), the appropriate α-methyleneamine (2.0 mmol) was added in one slot and the reaction mixture was stirred at room temperature for 3 h (monitored by TLC). It was then diluted with saturated NH_4Cl solution (25 mL), extracted with EtOAc (2 × 25 mL), the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

*3-(Benzylamino)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (**13a**).* Obtained as a single tautomer, pale yellow solid (603.6 mg, 88%)(82% in ethanol; 78% in DMF): mp 116−118 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3238, 2920, 1609, 1449, 1271, 734; ^1H NMR (400 MHz, DMSO-d_6) δ 11.67 (t, J = 6.0 Hz, 1H), 7.90−7.87 (m, 2H), 7.50−7.46 (m, 3H), 7.44−7.41 (m, 2H), 7.38−7.34 (m, 2H), 7.30−7.28 (m, 1H), 7.26−7.24 (m, 2H), 7.05 (d, J = 8.8 Hz, 2H), 5.84 (s, 1H), 4.48 (d, J = 6.0 Hz, 2H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 186.7, 166.2, 160.4, 139.7, 138.7, 130.8, 129.4, 128.7, 128.3, 127.3, 127.0, 126.9, 126.8, 114.1, 92.9, 55.3, 47.7; HRMS (ESI) m/z calcd for $C_{23}H_{22}NO_2$ $[M + H]^+$ 344.1651, found 344.1648.

*3-(Benzylamino)-3-(methylthio)-1-phenylprop-2-en-1-one (**13p**).* Obtained as a single tautomer, brown solid (487.6 mg, 81%): mp 88−90 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3227, 2114, 1574, 1294, 768; ^1H NMR (400 MHz, $CDCl_3$) δ 11.4 (br s, 1H), 7.83 (d, J = 8.8 Hz, 2H), 7.49 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.47 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.38 (d, J = 8.8 Hz, 2H), 7.15 (dd, J = 5.2 Hz, 3.6 Hz, 1H), 6.00 (s, 1H), 4.17 (dd, J = 6.4 Hz, 2.4 Hz, 2H), 2.36 (t, J = 2.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.7, 158.7, 138.4, 137.4, 135.4, 129.4, 128.74, 128.67, 128.5, 127.9, 95.0, 79.9, 73.0, 34.6; HRMS (ESI) m/z calcd for $C_{16}H_{13}ClNOS$ $[M + H]^+$ 302.0406, found 302.0403.

*3-(Benzo[d][1,3]dioxol-5-yl)-3-(prop-2-ynylamino)-1-(thiophen-2-yl)prop-2-en-1-one (**13q**).* Obtained as a single tautomer, brown solid (528.7 mg, 85%): mp 83−85 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3287, 2898, 2120, 1574, 1231, 773; ^1H NMR (400 MHz, $CDCl_3$) δ 10.91 (br s, 1H), 7.57 (d, J = 3.6 Hz, 1H), 7.48 (d, J = 3.2 Hz, 1H), 7.06 (t, J = 4.0 Hz, 1H), 7.00−6.96 (m, 2H), 6.89 (d, J = 8.0 Hz, 1H), 6.05 (s, 2H), 5.70 (s, 1H), 3.95 (dd, J = 7.2 Hz, 3.6 Hz, 2H), 2.30 (t, J = 2.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.1, 165.4, 149.2, 148.0, 147.0, 130.7, 128.5, 128.3, 127.9, 122.3, 108.7, 108.5, 101.8, 94.6, 79.9, 72.6, 34.4; HRMS (ESI) m/z calcd for $C_{17}H_{14}NO_3S$ $[M + H]^+$ 312.0694, found 312.0690.

*Synthesis of α-Hydroxyiminoimine **14a** from N-Benzylenaminone **13a**.* To a stirred solution of enaminone **13a** (343.1 mg, 1.0 mmol) in dry acetonitrile (3 mL), 82.8 mg (1.2 mmol) of sodium nitrite and 0.08 mL (1.5 mmol) of acetic acid were added and the reaction mixture was stirred at room temperature for 1 h (monitored by TLC). It was then neutralized with saturated $NaHCO_3$ solution (25 mL), extracted with EtOAc (2 × 25 mL) and the combined extracts were washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to afford crude

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14a, which was purified by column chromatography using EtOAc/hexane (2:3) as eluent.

*(2E,3E)-3-(Benzylimino)-2-(hydroxyimino)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**14a**).* Obtained as a single tautomer, pale yellow solid (632.4 mg, 85%): mp 53−55 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3251, 2923, 1641, 1594, 1325, 687; ^1H NMR (400 MHz, DMSO-d_6) δ 13.16 (s, 1H), 8.06 (d, J = 8.4 Hz, 2H), 7.69−7.65 (m, 3H), 7.59−7.56 (m, 2H), 7.39−7.35 (m, 2H), 7.34−7.32 (m, 2H), 7.26−7.25 (m, 1H), 6.99 (d, J = 8.4 Hz, 2H), 4.53 (q, J = 16.0 Hz, 2H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 189.0, 161.1, 159.1, 153.0, 139.7, 135.9, 133.1, 130.1, 128.4, 128.3, 128.2, 128.1, 127.8, 126.5, 114.0, 57.2, 55.2; HRMS (ESI) m/z calcd for $C_{23}H_{21}N_2O_3$ $[M + H]^+$ 373.1552, found 373.1548.

Base Mediated Intramolecular Cyclization of α-Hydroxyiminoimine 14a. *Synthesis of Imidazole **7a**.* To a stirred solution of α-hydroxyiminoimine **14a** (186.0 mg, 0.5 mmol) in dry acetonitrile (3 mL), 69.1 mg (0.5 mmol) of K_2CO_3 was added at room temperature, and the reaction mixture was heated with stirring at 80 °C for 3 h (monitored by TLC). It was then treated with saturated NH_4Cl solution (25 mL), extracted with EtOAc (2 × 25 mL), the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude imidazole **7a** thus obtained, was purified by column chromatography using EtOAc/hexane (3:7) as eluent.

*5-(4-Methoxyphenyl)-2-phenyl-1H-imidazol-4-yl)(phenyl)-methanone and (4-(4-Methoxyphenyl)-2-phenyl-1H-imidazol-5-yl)-(phenyl)methanone (**7a**).* Obtained as a 75:25 inseparable mixture of tautomers, pale yellow solid (153.9 mg, 87%): mp 150−152 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3264, 1592, 1571, 1423, 1244, 781; ^1H NMR (400 MHz, DMSO-d_6) δ 13.31 (br s, 0.25H), 13.11, (br s, 0.75H), 8.22−8.20 (m, 0.5H), 8.13−8.11 (m, 1.5H), 8.08−8.05 (m, 1.5H), 7.70 (d, J = 8.8 Hz, 1.5H), 7.61−7.56 (m, 1.5 H), 7.52−7.47 (m, 4H), 7.43−7.40 (m, 0.75H), 7.34−7.27 (m, 0.75H), 7.03 (d, J = 8.8 Hz, 1.5H), 6.71 (d, J = 8.8 Hz, 0.5H), 3.82 (s, 2.25H), 3.69 (s, 0.75H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 188.3, 186.2, 159.6, 158.8, 148.2, 147.6, 146.4, 144.9, 138.8, 138.6, 137.7, 135.4, 132.2, 131.9, 130.7, 130.4, 130.2, 129.7, 129.5, 129.3, 129.2, 128.9, 128.7, 128.1, 127.9, 126.4, 125.7, 121.8, 113.5, 113.1, 55.3, 55.0; HRMS (ESI) m/z calcd for $C_{23}H_{19}N_2O_2$ $[M + H]^+$ 355.1447, found 355.1442.

General Procedure for Sequential One-Pot Synthesis of 2,4,5-Trisubstituted Imidazoles 7a−k from Monothio-1,3-diketones 1a−h. To a stirred solution of monothio-1,3-diketone **1** (1.0 mmol) in dry acetonitrile (5 mL), appropriate α-methyleneamine (1.0 mmol) was added in one slot and the reaction mixture was further stirred at room temperature for 3 h. After complete consumption of starting materials (monitored by TLC), sodium nitrite (82.8 mg, 1.2 mmol) and acetic acid (0.08 mL, 1.5 mmol) were added to the reaction mixture, followed by further stirring for 1 h at room temperature. After completion of the reaction (monitored by TLC), 691.0 mg (5.0 mmol) of K_2CO_3 was added and the reaction mixture was heated at 80 °C for 5−8 h (monitored by TLC). After cooling to room temperature, it was then treated with saturated NH_4Cl solution (2 × 25 mL), extracted with EtOAc (3 × 25 mL), the combined organic extract was washed with water (3 × 25 mL), brine (25 mL), dried (Na_2SO_4), and evaporated to give crude residues, which on purification by column chromatography (EtOAc/hexane as eluent) afforded the pure imidazoles **7**. The spectral and analytical data for all newly synthesized imidazoles **7b−k** is given below.

*Furan-2-yl(5-(1-methyl-1H-pyrrol-2-yl)-2-(4-(trifluoromethyl)-phenyl)-1H-imidazol-4-yl)methanone and Furan-2-yl(4-(1-methyl-1H-pyrrol-2-yl)-2-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)-methanone (**7b**).* Obtained as a 50:50 inseparable mixture of tautomers, yellow solid (334.9 mg, 87%): mp 85−87 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3143, 1615, 1465, 1324, 1115, 847; ^1H NMR (400 MHz, $CDCl_3$) δ 11.20 (br s, 0.5H), 10.05 (br s, 0.5H), 8.24−8.20 (m, 1.5H), 8.05 (d, J = 8.0 Hz, 1H), 7.75−7.72 (m, 2H), 7.65 (d, J = 0.8 Hz, 0.5H), 7.52 (d, J = 0.8 Hz, 0.5H), 6.79 (t, J = 2.4 Hz, 0.5 H), 6.69 (t, J = 2.4 Hz, 0.5H), 6.61−6.60 (m, 1H), 6.44 (dd, J = 3.6 Hz, 1.6 Hz, 0.5H), 6.40 (dd, J = 3.6 Hz, 1.6 Hz, 0.5H), 6.33 (dd, J = 3.6 Hz, 1.6 Hz, 0.5H), 6.18 (t, J = 2.8 Hz, 0.5H), 6.14 (t, J = 2.8 Hz, 0.5H), 3.63 (s, 1.5H), 3.57 (s, 1.5H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.7, 171.7, 152.1, 151.4, 147.9, 147.0, 144.5, 141.4, 137.6, 132.8, 132.2, 131.7, 131.2, 131.0, 128.5, 126.9, 126.1, 126.04, 126.0, 125.9, 125.42, 125.38, 125.1, 124.6, 122.72, 122.67, 122.5, 121.7, 119.9, 112.7, 112.6, 112.3, 111.4, 108.5, 108.2, 35.0, 34.9; HRMS (ESI) m/z calcd for C20H15F3N3O2 $[M + H]^+$ 386.1116, found 386.1107.

*(2-(Furan-2-yl)-5-(2-methoxyphenyl)-1H-imidazol-4-yl)-(thiophen-2-yl)methanone and (2-(Furan-2-yl)-4-(2-methoxyphenyl)-1H-imidazol-5-yl)(thiophen-2-yl)methanone (**7c**).* Obtained as a single tautomer, pale yellow solid (287.0 mg, 82%): mp 110−112 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3270, 1634, 1427, 1247, 837; ^1H NMR (400 MHz, DMSO-d_6) δ 13.28 (s, 1H), 8.45 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 7.94 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.86 (t, J = 0.8 Hz, 1H), 7.46−741 (m, 2H), 7.24 (dd, J = 4.8 Hz, 4.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 7.06−7.01 (m, 2H), 6.68 (dd, J = 3.2 Hz, 1.6 Hz, 1H), 3.70 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 178.4, 156.9, 144.9, 143.7, 143.5, 137.8, 136.1, 134,8, 134.4, 134.2, 131.4, 130.3, 127.9, 119.8, 118.7, 111.8, 111.2, 108.5, 55.4; HRMS (ESI) m/z calcd for $C_{19}H_{15}N_2O_3S$ $[M + H]^+$ 351.0803, found 351.0787.

*Furan-2-yl(2-(2-methoxyphenyl)-5-(1-methyl-1H-pyrrol-2-yl)-1H-imidazol-4-yl)methanone and Furan-2-yl(2-(2-methoxyphenyl)-4-(1-methyl-1H-pyrrol-2-yl)-1H-imidazol-5-yl)methanone (**7d**).* Obtained as a 55:45 inseparable mixture of tautomers, yellow solid (281.0 mg, 81%): mp 90−92 °C; R_f 0.3 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3388, 1606, 1485, 1205, 1015; ^1H NMR (400 MHz, $CDCl_3$) δ 11.61 (br s, 0.45H), 10.52 (br s, 0.55H), 8.49−8.45 (m, 1H), 8.27 (d, J = 3.6 Hz, 0.55H), 7.66 (s, 0.55H), 7.55 (s, 0.45H), 7.44−7.38 (m, 1H), 7.18−7.11 (m, 1H), 7.08−7.04 (m, 1H), 6.87−6.86 (m, 1H), 6.70 (s, 0.45H), 6.67 (dd, J = 3.6 Hz, 1.6 Hz, 0.45H), 6.60 (dd, J = 3.2 Hz, 1.6 Hz, 0.55H), 6.50 (dd, J = 3.2 Hz, 1.6 Hz, 0.45H), 6.40 (dd, J = 3.6 Hz, 1.6 Hz, 0.55H), 6.26 (t, J = 3.2 Hz, 0.55H), 6.17 (t, J = 3.2 Hz, 0.45H), 4.11 (s, 1.35H), 4.01 (s, 1.65H), 3.72 (s, 1.35H), 3.62 (s, 1.65H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.7, 169.9, 156.7, 156.3, 152.9, 152.4, 146.7, 146.6, 145.5, 144.0, 141.5, 136.7, 131.2, 130.6, 129.8, 128.9, 128.8, 126.5, 126.0, 124.8, 124.7, 122.7, 122.0, 121.9, 121.8, 118.3, 117.6, 117.2, 112.9, 112.6, 112.1, 111.5, 111.4, 110.9, 108.1, 108.0, 56.2, 56.0, 35.6, 35.0; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_3O_3$ $[M + H]^+$ 348.1348, found 348.1336.

*(2,5-Di(thiophen-2-yl)-1H-imidazol-4-yl)(thiophen-2-yl)-methanone and (2,4-Di(thiophen-2-yl)-1H-imidazol-5-yl)(thiophen-2-yl)methanone (**7e**).* Obtained as a single tautomer, yellow solid (242.1 mg, 71%): mp 76−78 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3096, 1601, 1408, 1227, 700; ^1H NMR (400 MHz, DMSO-d_6) δ 13.3, (br s, 1H), 8.44 (d, J = 3.2 Hz, 1H), 8.02 (d, J = 4.8 Hz, 1H), 7.92 (d, J = 3.2 Hz, 1H), 7.88 (d, J = 3.2 Hz, 1H), 7.73 (d, J = 4.8 Hz, 1H), 7.69 (d, J = 4.8 Hz, 1H), 7.28 (t, J = 4.0 Hz, 1H), 7.25−7.20 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 178.0, 142.8, 141.6, 135.5, 135.1, 134.2, 132.6, 132.5, 129.8, 129.0, 128.9, 128.2, 127.9, 127.0, 126.3; HRMS (ESI) m/z calcd for $C_{16}H_{11}N_2OS_3$ $[M + H]^+$ 343.0034, found 343.0028.

*(5-Butyl-2-(thiophen-2-yl)-1H-imidazol-4-yl)(4-methoxyphenyl)-methanone and (4-Butyl-2-(thiophen-2-yl)-1H-imidazol-5-yl)(4-methoxyphenyl)methanone (**7f**).* Obtained as a 90:10 inseparable mixture of tautomers, yellow solid (227.8 mg, 67%): mp 81−83 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3244, 1594, 1380, 1252, 701; ^1H NMR (400 MHz, DMSO-d_6) δ 13.03, (br s, 0.1H), 12.95 (br s, 0.9H), 8.32 (d, J = 8.8 Hz, 1.8H), 7.88 (d, J = 2.4 Hz, 0.1H), 7.69 (d, J = 8.8 Hz, 0.2H), 7.61 (d, J = 3.6 Hz, 1H), 7.57 (d, J = 4.8 Hz, 0.9H), 7.15 (dd, J = 4.8 Hz, 4.0 Hz, 1H);, 7.09−7.03 (m, 2H), 3.85 (s, 3H), 2.98 (t, J = 7.6 Hz, 2H), 1.65 (quin, J = 7.6 Hz, 1.8H), 1.51−1.46 (m, 0.2H), 1.40−1.30 (m, 2H), 0.91 (t, J = 7.2 Hz, 2.7H), 0.85 (t, J = 7.2 Hz, 0.3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 185.9, 162.2, 142.0, 139.6, 135.8, 133.5, 132.5, 131.2, 128.0, 126.7, 124.7, 113.2, 55.4, 31.1, 25.1, 22.0, 13.7; HRMS (ESI) m/z calcd for $C_{19}H_{21}N_2O_2S$ $[M + H]^+$ 341.1324, found 341.1319.

*1-(5-(4-Methoxyphenyl)-2-phenyl-1H-imidazol-4-yl)ethanone and 1-(4-(4-Methoxyphenyl)-2-phenyl-1H-imidazol-5-yl)ethanone (**7g**).* Obtained as a 75:25 inseparable mixture of tautomers, yellow solid (189.8 mg, 65%): mp 195−197 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3273, 1634, 1497, 1247, 1030, 837; ^1H NMR (400 MHz, DMSO-d_6) δ 12.97, (br s, 0.25H), 12.95 (br s, 0.75H),

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8.19−8.17 (m, 0.5H), 8.09−8.07 (m, 1.5H), 7.74 (d, J = 8.8 Hz, 1.5H), 7.67 (d, J = 8.8 Hz, 0.5H), 7.51−7.46 (m, 2H), 7.44−7.40 (m, 1H), 7.05−7.00 (m, 2H), 3.83 (s, 2.25H), 3.82 (s, 0.75H), 2.53 (s, 2.25H), 2.28 (s, 0.75H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 194.0, 187.7, 159.7, 159.4, 147.7, 147.6, 144.7, 136.4, 135.8, 130.9, 130.8, 129.7, 129.5, 129.2, 128.8, 128.7, 128.4, 126.9, 126.5, 125.6, 121.6, 113.3, 55.2, 55.1, 28.4, 28.0; HRMS (ESI) m/z calcd for $C_{18}H_{17}N_2O_2$ $[M + H]^+$ 293.1290, found 293.1287.

*Ethyl 4-(4-chlorobenzoyl)-5-(4-methoxyphenyl)-1H-imidazole-2-carboxylate and Ethyl 5-(4-chlorobenzoyl)-4-(4-methoxyphenyl)-1H-imidazole-2-carboxylate (**7h**).* Obtained as a 75:25 inseparable mixture of tautomers, yellow solid (261.1 mg, 68%): mp 175−177 °C; R_f 0.3 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3398, 2958, 1680, 1601, 1426, 1259; ^1H NMR (400 MHz, $CDCl_3$) δ 11.05 (br s, 0.25H), 10.98 (br s, 0.75H), 8.10 (d, J = 8.4 Hz, 1.5H), 7.63 (d, J = 8.8 Hz, 1.5H), 7.50 (d, J = 8.0 Hz, 0.5H), 7.39 (d, J = 8.4 Hz, 1.5H), 7.25 (d, J = 8.4 Hz, 0.5H), 7.16 (d, J = 8.0 Hz, 0.5H), 6.93 (d, J = 8.4 Hz, 1.5H), 6.67 (d, J = 8.4 Hz, 0.5H), 4.51−4.40 (m, 2H), 3.83 (s, 2.25H), 3.75 (s, 0.75H), 1.44−1.37 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 181.9, 169.5, 162.9, 139.9, 135.2, 133.4, 131.3, 130.3, 129.1, 127.1, 126.1, 122.1, 114.3, 62.6, 55.5, 14.2; HRMS (ESI) m/z calcd for $C_{20}H_{18}ClN_2O_4$ $[M + H]^+$ 385.0955 and 387.0926, found 385.0945 and 387.0917.

*Ethyl 4-(4-methoxybenzoyl)-5-(thiophen-2-yl)-1H-imidazole-2-carboxylate and Ethyl 5-(4-methoxybenzoyl)-4-(thiophen-2-yl)-1H-imidazole-2-carboxylate (**7i**).* Obtained as a single tautomer, yellow solid (252.7 mg, 71%): mp 150−152 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3358, 1788, 1694, 1254, 709; ^1H NMR (400 MHz, $CDCl_3$) δ 9.84 (br s, 1H), 7.83 (d, J = 8.8 Hz, 2H), 7.46 (dd, J = 3.6 Hz, 0.8 Hz, 1H), 7.35 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.04 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 4.09 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.7, 164.0, 150.9, 148.7, 131.1, 130.7, 129.5, 129.0, 128.7, 127.8, 123.5, 116.2, 114.2, 64.4, 55.7, 13.7; HRMS (ESI) m/z calcd for $C_{18}H_{17}N_2O_4S$ $[M + H]^+$ 357.0909, found 357.0918.

*(5-(4-(Dimethylamino)phenyl)-2-vinyl-1H-imidazol-4-yl)-(thiophen-2-yl)methanone and (4-(4-(Dimethylamino)phenyl)-2-vinyl-1H-imidazol-5-yl)(thiophen-2-yl)methanone (**7j**).* Obtained as a single tautomer, pale yellow solid (229.3 mg, 71%): mp 112−114 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3210, 2981, 1608, 1494, 1409, 1150; ^1H NMR (400 MHz, DMSO-d_6) δ 12.79 (s, 1H), 8.37 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.92 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.67 (d, J = 8.8 Hz, 2H), 7.21 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 6.78 (d, J = 8.8 Hz, 2H), 6.66 (dd, J = 18.0 Hz, 11.6 Hz, 1H), 6.19 (dd, J = 17.6 Hz, 0.8 Hz, 1H), 5.51 (dd, J = 11.2 Hz, 0.8 Hz, 1H), 2.97 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 178.4, 150.5, 144.1, 143.7, 139.3, 134.6, 134.5, 133.7, 130.0, 127.6, 125.7, 117.9, 116.2, 111.1, 39.8; HRMS (ESI) m/z calcd for $C_{18}H_{18}N_3OS$ $[M + H]^+$ 324.1171, found 324.1166.

*(4-Chlorophenyl)(5-(4-methoxyphenyl)-2-vinyl-1H-imidazol-4-yl)methanone and (4-Chlorophenyl)(4-(4-methoxyphenyl)-2-vinyl-1H-imidazol-5-yl)methanone (**7k**).* Obtained as a 80:20 inseparable mixture of tautomers, yellow solid (273.7 mg, 81%): mp 60−62 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3224, 2834, 1607, 1586, 1484, 1250; ^1H NMR (400 MHz, DMSO-d_6) δ 13.04 (br s, 0.2H), 12.97 (br s, 0.8H), 8.28 (d, J = 8.8 Hz, 0.2H), 8.08 (d, J = 8.0 Hz, 1.6H), 7.91−7.89 (m, 0.4H), 7.66 (d, J = 8.4 Hz, 1.6H), 7.54 (d, J = 8.0 Hz, 1.6H), 7.33−7.30 (m, 0.8H), 7.02 (d, J = 8.4 Hz, 1.6H), 6.72 (d, J = 5.6 Hz, 0.4H), 6.63 (dd, J = 17.6 Hz, 11.6 Hz, 0.8H), 6.30 (d, J = 17.6 Hz, 0.2H), 6.14 (d, J = 17.6 Hz, 0.8H), 5.58 (d, J = 11.2 Hz, 0.2H), 5.50 (d, J = 11.2 Hz, 0.8H), 3.86 (s, 0.6H), 3.81 (s, 2.44H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 186.9, 159.7, 144.5, 138.6, 137.3, 136.7, 134.8, 132.0, 130.5, 127.9, 125.9, 121.6, 118.2, 113.5, 55.3; HRMS (ESI) m/z calcd for $C_{19}H_{16}ClN_2O_2$ $[M + H]^+$ 339.0900 and 341.0871, found 339.0900 and 341.0862.

One-Pot Synthesis of Imidazole 12a from N,S-Acetal 10a. To a stirred solution of N,S-acetal **10a**[31] (283.1 mg, 1.0 mmol) in dry acetonitrile (5 mL), 82.8 mg (1.2 mmol) of sodium nitrite and acetic acid (0.08 mL, 1.5 mmol) were added and the reaction mixture was stirred at room temperature for 1 h (monitored by TLC), followed by addition of 691.0 mg (5.0 mmol) of K_2CO_3. It was then heated at 80 °C for 3 h (monitored by TLC) and followed by subsequent workup and purification as described for imidazoles **7**.

*(5-(Methylthio)-2-phenyl-1H-imidazol-4-yl)(phenyl)methanone and (4-(Methylthio)-2-phenyl-1H-imidazol-5-yl)(phenyl)methanone (**12a**).*[30a] Obtained as a single tautomer, pale yellow solid (211.6 mg, 72%): mp 213-215 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3247, 1594, 1455, 1284, 701; ^1H NMR (400 MHz, $CDCl_3$) δ 11.10 (br s, 1H), 8.07−8.05 (m, 2H), 7.80 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.55−7.51 (m, 2H), 7.44−7.43 (m, 3H), 2.59 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.3, 150.2, 149.2, 138.6, 132.4, 130.4, 129.1, 128.71, 128.70, 128.1, 126.6, 15.1; HRMS (ESI) m/z calcd for $C_{17}H_{15}N_2OS$ $[M + H]^+$ 295.0905, found 295.0899.

General Procedure for *N*-Methylation of *NH*-Imidazoles 7: Synthesis of 1-*N*-Methy-2,5-bishet(aryl)/alkyl-4-het(aroyl) imidazoles 8a−k, 8p. To a stirred solution of 1(3)-*NH*- imidazoles **7** (0.3 mmol) in dry acetonitrile (3 mL), 41.4 mg (0.3 mmol) of K_2CO_3 was added and the reaction mixture was stirred at room temperature for 1 h, followed by addition of MeI (0.018 mL, 0.3 mmol) and further stirring for 2 h at room temperature (monitored by TLC). The reaction mixture was treated with saturated NH_4Cl solution (25 mL), extracted with EtOAc (2 × 25 mL), the combined organic extracts were washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and evaporated to give crude *N*-methylimidazoles **8**, which were purified by column chromatography using EtOAc/hexane as eluent.

*(5-(4-Methoxyphenyl)-1-methyl-2-phenyl-1H-imidazol-4-yl)-(phenyl)methanone (**8a**).* Obtained from **7a**, pale yellow solid (100.5 mg, 91%): mp 99−101 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2864, 1635, 1248, 1172, 714; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22−8.20 (m, 2H), 7.76−7.73 (m, 2H), 7.53−7.45 (m, 4H), 7.40−7.37 (m, 4H), 6.98 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 3.57 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.9, 160.3, 147.7, 140.8, 138.5, 137.1, 132.0, 131.9, 130.8, 130.5, 129.4, 129.3, 128.8, 128.0, 121.9, 114.2, 55.5, 33.6; HRMS (ESI) m/z calcd for $C_{24}H_{21}N_2O_2$ $[M + H]^+$ 369.1603, found 369.1590.

*Furan-2-yl(1-methyl-5-(1-methyl-1H-pyrrol-2-yl)-2-(4-(trifluoromethyl)phenyl)-1H-imidazol-4-yl)methanone (**8b**).* Obtained from **7b**, yellow solid (111.3 mg, 93%): mp 112−114 °C; R_f 0.6 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2936, 1643, 1475, 1328, 1129, 865; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 3.6 Hz, 0.8 Hz, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.64 (dd, J = 1.6 Hz, 0.8 Hz, 1H), 6.87 (t, J = 2.4 Hz, 1H), 6.55 (dd, J = 3.6 Hz, 1.6 Hz, 1H), 6.284−6.280 (m, 2H), 3.62 (s, 3H), 3.55 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.3, 152.0, 146.7, 146.5, 138.6, 133.8, 132.7, 131.4, 131.1, 129.2, 125.7 (q, J_{C-F} = 4.0 Hz), 124.6, 121.8, 120.1, 112.0, 111.9, 108.2, 34.6, 33.3; HRMS (ESI) m/z calcd for $C_{21}H_{17}F_3N_3O_2$ $[M + H]^+$ 400.1273, found 400.1261.

*(2-(Furan-2-yl)-5-(2-methoxyphenyl)-1-methyl-1H-imidazol-4-yl)-(thiophen-2-yl)methanone (**8c**).* Obtained from **7c**, pale yellow solid (98.2 mg, 90%): mp 148−150 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2995, 1670, 1499, 1250, 937; ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 2.8 Hz, 1H), 7.53−7.50 (m, 2H), 738 (td, J = 8.8 Hz, 1.6 Hz, 1H), 7.31 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.05 (t, J = 4.4 Hz, 1H), 7.00 (t, 7.6 Hz, 1H), 6.96−6.93 (m, 2H), 6.51 (dd, J = 3.2 Hz, 2.0 Hz, 1H), 3.71 (s, 3H), 3.56 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.2, 157.6, 145.8, 143.9, 143.2, 139.1, 137.5, 136.9, 135.2, 133.8, 133.1, 131.3, 127.7, 120.9, 118.2, 111.8, 111.3, 110.7, 55.7, 32.6; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_3S$ $[M + H]^+$ 365.0960, found 365.0954.

*Furan-2-yl(2-(2-methoxyphenyl)-1-methyl-5-(1-methyl-1H-pyrrol-2-yl)-1H-imidazol-4-yl)methanone (**8d**).* Obtained from **7d**, pale yellow solid (98.2 mg, 96%): mp 155−157 °C; R_f 0.5 (4:6 EtOAc/hexane); IR (neat, cm^{-1}) 2965, 1630, 1475, 1254, 1019; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 3.6 Hz, 0.8 Hz, 1H), 7.61−7.58 (m, 2H), 7.49 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.12 (td, J = 7.6 Hz, 0.8 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.86 (t, J = 2.0 Hz, 1H), 6.50 (dd, J = 3.6 Hz, 1.6 Hz, 1H), 6.29−6.25 (m, 2H), 3.86 (s, 3H), 3.56 (s, 3H), 3.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.8, 157.8, 152.4, 146.5, 146.4, 138.4, 132.6, 131.6, 124.3, 121.8, 121.2, 120.9, 119.9,

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112.0, 111.6, 111.2, 108.0, 55.7, 34.7, 32.2; HRMS (ESI) m/z calcd for $C_{21}H_{20}N_3O_3$ $[M + H]^+$ 362.1505, found 362.1494.

*(1-Methyl-2,5-di(thiophen-2-yl)-1H-imidazol-4-yl)(thiophen-2-yl)-methanone (**8e**).* Obtained from **7e**, pale yellow solid (95.0 mg, 89%): mp 90−92 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2928, 1629, 1511, 1416, 1232, 828; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.64 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.56 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.50−7.48 (m, 2H), 7.30 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.20−7.14 (m, 3H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.9, 143.6, 142.7, 138.0, 135.5, 134.3, 132.8, 132.5, 130.9, 128.84, 128.80, 127.82, 127.81, 127.80, 127.4, 127.1, 33.4; HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2OS_3$ $[M + H]^+$ 357.0190, found 357.0173.

*(5-Butyl-1-methyl-2-(thiophen-2-yl)-1H-imidazol-4-yl)(4-methoxyphenyl)methanone (**8f**).* Obtained from **7f**, pale yellow semisolid (89.2 mg, 84%): R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2827, 1635, 1497, 1248, 896; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 9.2 Hz, 2H), 7.42 (dd, J = 5.2 Hz, 0.8 Hz, 1H), 7.37 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.13 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 6.95 (d, J = 9.2 Hz, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.09 (t, J = 8.0 Hz, 2H), 1.69−1.63 (m, 2H), 1.54−1.44 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.6, 162.9, 142.8, 140.7, 136.7, 133.2, 132.7, 131.7, 127.6, 127.2, 127.0, 113.3, 55.6, 31.8, 31.3, 24.8, 22.9, 14.0; HRMS (ESI) m/z calcd for $C_{20}H_{23}N_2O_2S$ $[M + H]^+$ 355.1480, found 355.1474.

*1-(5-(4-Methoxyphenyl)-1-methyl-2-phenyl-1H-imidazol-4-yl)-ethanone (**8g**).* Obtained from **7g**, off white solid (83.5 mg, 91%): mp 102−104 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2928, 1629, 1511, 1416, 1232, 828; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70−7.68 (m, 2H), 7.52−7.44 (m, 3H), 7.37 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 3.47 (s, 3H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.7, 160.4, 147.7, 138.4, 137.4, 131.9, 130.4, 129.5, 129.3, 128.9, 121.7, 114.2, 55.5, 33.4, 28.1; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1447, found 307.1440.

*Ethyl 4-(4-chlorobenzoyl)-5-(4-methoxyphenyl)-1-methyl-1H-imidazole-2-carboxylate (**8h**).* Obtained from **7h**, off white solid (105.0 mg, 88%): mp 90−92 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2928, 1716, 1650, 1482, 1254, 902; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.8 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 7.0 (d, J = 8.8 Hz, 2H), 4.47 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 1.45 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.9, 160.8, 159.6, 143.1, 138.9, 137.3, 136.14, 136.05, 132.3, 131.9, 128.5, 120.1, 114.3, 62.1, 55.5, 34.1, 14.5; HRMS (ESI) m/z calcd for $C_{21}H_{20}ClN_2O_4$ $[M + H]^+$ 399.1112 and 401.1082, found 399.1108 and 401.1074.

*Ethyl 4-(4-methoxybenzoyl)-1-methyl-5-(thiophen-2-yl)-1H-imidazole-2-carboxylate (**8i**).* Obtained from **7i**, off white solid (98.7 mg, 89%): mp 108−110 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 2874, 1736, 1588, 1496, 1293, 839; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.8 Hz, 2H), 7.38 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.14 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 6.96 (dd, J = 5.2 Hz, 4.0 Hz, 1H), 6.81 (d, J = 8.8 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H), 3.28 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.5, 163.8, 150.2, 148.9, 131.7, 131.3, 130.4, 129.3, 127.5, 126.0, 124.5, 118.7, 113.9, 64.4, 55.6, 29.2, 13.9; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_2O_4S$ $[M + H]^+$ 371.1066, found 371.1072.

*(5-(4-(Dimethylamino)phenyl)-1-methyl-2-vinyl-1H-imidazol-4-yl)(thiophen-2-yl)methanone (**8j**).* Obtained from **7j**, yellow solid (88.9 mg, 88%): mp 88−90 °C; R_f 0.6 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 2926, 1621, 1406, 1218, 855; ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.60 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.29 (d, J = 8.8 Hz, 2H), 7.12 (dd, J = 4.8 Hz, 4.0 Hz, 1H), 6.79 (d, J = 8.8 Hz, 2H), 6.70 (dd, J = 17.2 Hz, 11.2 Hz, 1H), 6.40 (dd, J = 17.2 Hz, 1.6 Hz, 1H), 5.57 (dd, J = 10.8 Hz, 1.6 Hz, 1H), 3.52 (s, 3H), 3.01 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 180.9, 167.5, 151.4, 147.6, 134.8, 129.6, 129.1, 127.6, 127.3, 122.3, 116.3, 111.5, 110.0, 40.2, 33.2; HRMS (ESI) m/z calcd for $C_{19}H_{20}N_3OS$ $[M + H]^+$ 338.1327, found 338.1320.

*(4-Chlorophenyl)(5-(4-methoxyphenyl)-1-methyl-2-vinyl-1H-imidazol-4-yl)methanone and (4-Chlorophenyl)(4-(4-methoxyphenyl)-1-methyl-2-vinyl-1H-imidazol-5-yl)methanone (**8k**).* Obtained from **7k**, as a 77:23 inseparable mixture of tautomers, yellow semisolid (87.6 mg, 83%): mp 88−90 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2922, 1643, 1586, 1455, 1246, 903; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 1.54H), 7.54 (d, J = 8.4 Hz, 0.46H), 7.35 (d, J = 8.4 Hz, 1.54H), 7.29 (d, J = 8.4 Hz, 1.54H), 7.16 (d, J = 8.4 Hz, 0.46H), 7.11 (d, J = 8.4 Hz, 0.46H), 6.97 (d, J = 8.8 Hz, 1.54H), 6.76−6.65 (m, 1H), 6.62 (d, J = 8.8 Hz, 0.46H), 6.49 (dd, J = 17.2 Hz, 1.6 Hz, 0.23H), 6.32 (dd, J = 17.2 Hz, 1.6 Hz, 0.77H), 5.69 (dd, J = 11.2 Hz, 1.6 Hz, 0.23H), 5.58 (dd, J = 11.2 Hz, 1.6 Hz, 0.77H), 3.86 (s, 0.69H), 3.85 (s, 2.31H), 3.72 (s, 0.69H), 3.51 (s, 2.31H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.1, 186.6, 160.3, 159.6, 149.3, 149.1, 145.0, 140.4, 138.8, 138.3, 136.8, 136.7, 136.6, 132.3, 131.9, 131.4, 130.8, 128.3, 128.2, 126.8, 126.3, 123.1, 123.0, 122.2, 121.3, 120.8, 114.1, 113.6, 55.5, 55.4, 32.3, 31.4; HRMS (ESI) m/z calcd for $C_{20}H_{18}ClN_2O_2$ $[M + H]^+$ 353.1057 and 355.1027, found 353.1061 and 355.1034.

*(4-Chlorophenyl)(2-ethynyl-1-methyl-5-(thiophen-2-yl)-1H-imidazol-4-yl)methanone and (4-Chlorophenyl)(2-ethynyl-1-methyl-4-(thiophen-2-yl)-1H-imidazol-5-yl)methanone (**8p**).* Obtained from **7p**, as a 60:40 inseparable mixture of tautomers, yellow solid (90.9 mg, 93%): mp 85−87 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2925, 2119, 1644, 1586, 1475, 1087; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.8 Hz, 1.2H), 7.68 (d, J = 8.8 Hz, 0.8H), 7.54 (dd, J = 5.2 Hz, 1.2 Hz, 0.6H), 7.39 (d, J = 8.8 Hz, 1.2H), 7.28−7.27 (m, 1.4H), 7.19 (dd, J = 5.2 Hz, 1.2 Hz, 0.4H), 7.16 (dd, J = 5.2 Hz, 3.6 Hz, 0.6H), 6.72 (dd, J = 5.2 Hz, 3.6 Hz, 0.4H), 6.66 (dd, J = 3.6 Hz, 1.2 Hz, 0.4H), 3.88 (s, 1.2H), 3.70 (s, 1.8H), 3.49 (s, 0.4H), 3.42 (s, 0.6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.4, 186.0, 141.5, 140.0, 139.0, 138.6, 136.1, 135.8, 135.3, 134.7, 132.7, 132.2, 131.4, 131.3, 131.0, 129.0, 128.9, 128.5, 128.3, 128.0, 127.5, 127.3, 127.1, 126.4, 84.1, 82.6, 72.8, 72.4, 33.9, 32.8; HRMS (ESI) m/z calcd for $C_{17}H_{12}ClN_2OS$ $[M + H]^+$ 327.0359 and 329.0329, found 327.0352 and 329.0318.

General Procedure for the Synthesis of 4(5)-[2-(4-Methoxybenzyloxy)phenyl]-2,5(4) substituted imidazoles 7m′−o′. The imidazoles **7m′−7o′** were prepared from the respective monothioketones **1j−l** (1.0 mmol) and the appropriate α-methyleneamine (1.0 mmol) and sodium nitrite (82.2 mg, 1.2 mmol) following the general one-pot procedure as described above.

*(5-(2-(4-Methoxybenzyloxy)phenyl)-2-(4-chlorophenyl)-1H-imidazol-4-yl)(thiophen-2-yl)methanone and (4-(2-(4-Methoxybenzyloxy)phenyl)-2-(4-chlorophenyl)-1H-imidazol-5-yl)-(thiophen-2-yl)methanone (**7m′**).* Obtained as a single tautomer, yellow solid (410.0 mg, 82%): mp 140−142 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3373, 1608, 1515, 1351, 1235, 749; ^1H NMR (400 MHz, DMSO-d_6) δ 13.30 (br s, 1H), 8.44 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.98 (dd, J = 4.8 Hz, 0.8 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.52−7.44 (m, 2H), 7.27−7.22 (m, 4H), 7.08 (t, J = 7.2 Hz, 1H), 6.67 (d, J = 8.4 Hz, 2H), 5.00 (s, 2H), 3.65 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 178.2, 158.7, 156.2, 143.8, 143.3, 136.4, 135.1, 134.8, 134.6, 133.4, 131.5, 130.4, 129.2, 129.0, 128.5, 127.8, 127.0, 120.0, 119.2, 113.3, 112.5, 69.4, 54.9; HRMS (ESI) m/z calcd for $C_{28}H_{22}ClN_2O_3S$ $[M + H]^+$ 501.1040 and 503.1010, found 501.1026 and 503.0994.

*(5-(2-(4-Methoxybenzyloxy)phenyl)-2-(thiophen-2-yl)-1H-imidazol-4-yl)(thiazol-2-yl)methanone and (4-(2-(4-Methoxybenzyloxy)-phenyl)-2-(thiophen-2-yl)-1H-imidazol-5-yl)(thiazol-2-yl)-methanone (**7n′**).* Obtained as a 75:25 inseparable mixture of tautomers, yellow solid (402.0 mg, 85%): mp 72−74 °C; R_f 0.4 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3279, 1633, 1514, 1481, 1240, 835; ^1H NMR (400 MHz, DMSO-d_6) δ 13.43 (s, 0.75H), 13.28 (s, 0.25H), 8.12−8.08 (m, 1.5H), 7.96−7.84 (m, 0.5H), 7.71−7.64 (m, 1.5H), 7.52−7.44 (m, 2H), 7.28−7.20 (m, 3H), 7.13-.7.07 (m, 1.5H), 7.02−6.93 (m, 1H), 6.71 (d, J = 8.0 Hz, 0.5H), 6.66 (d, J = 8.0 Hz, 1.5H), 4.94 (s, 1.5H), 4.72 (s, 0.5H), 3.68 (s, 0.75H), 3.65 (s, 2.25H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 176.2, 162.9, 158.7, 156.0, 143.8, 141.3, 135.7, 135.5, 132.7, 131.1, 130.7, 129.4, 128.3, 128.2, 127.5, 127.3, 125.6, 120.2, 118.7, 113.4, 112.6, 69.5, 54.9; HRMS (ESI) m/z calcd for $C_{25}H_{20}N_3O_3S_2$ $[M + H]^+$ 474.0946, found 474.0943.

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*(5-(2-(4-Methoxybenzyloxy)phenyl)-2-(2-methoxyphenyl)-1H-imidazol-4-yl)(pyridin-3-yl)methanone and (4-(2-(4-Methoxybenzyloxy)phenyl)-2-(2-methoxyphenyl)-1H-imidazol-5-yl)(pyridin-3-yl)methanone (**7o′**).* Obtained as a 90:10 inseparable mixture of tautomers, yellow solid (378.0 mg, 77%): mp 80−82 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3413, 2924, 1643, 1414, 1239, 748; ^1H NMR (400 MHz, DMSO-d_6) δ 12.43 (s, 0.9H), 12.08 (s, 0.1H), 9.18 (d, J = 1.6 Hz, 0.9H), 8.71 (dd, J = 4.4 Hz, 0.8 Hz, 0.9H), 8.51−8.48 (m, 0.2H), 8.35 (dt, J = 8.0 Hz, 2.0 Hz, 0.9H), 8.10 (dd, J = 7.6 Hz, 1.6 Hz, 0.1H), 7.98 (dd, J = 7.6 Hz, 1.6 Hz, 0.9H), 7.70 (d, J = 7.6 Hz, 0.1H), 7.51−7.47 (m, 1.8H), 7.44−7.39 (m, 1.8H), 7.24−7.16 (m, 3.8H), 7.13−7.02 (m, 2.2H), 6.97−6.93 (m, 0.2H), 6.83 (d, J = 8.8 Hz, 0.2H), 6.72 (d, J = 8.4 Hz, 0.2H), 6.68 (d, J = 8.8 Hz, 1.8H), 4.97 (s, 1.8H), 4.57 (s, 0.2H), 3.98 (s, 0.3H), 3.87 (s, 2.7H), 3.72 (s, 0.3H), 3.66 (s, 2.7H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 186.3, 158.7, 156.3, 156.1, 151.8, 150.8, 142.9, 137.3, 135.9, 134.9, 133.9, 131.5, 130.5, 130.2, 129.1, 128.9, 128.5, 123.1, 120.7, 120.1, 119.2, 118.0, 113.4, 112.5, 111.7, 69.5, 55.5, 54.9; HRMS (ESI) m/z calcd for $C_{30}H_{26}N_3O_4$ $[M + H]^+$ 492.1923, found 492.1923.

General Procedure for deprotection of 4(5)-[2-(4-Methoxybenzyloxy)phenyl] imidzoles 7m′−o′ to (2-(Hydroxyphenyl)-2,5(4)-substituted imidazoles 7m−o. To a stirred solution of 4(5)-[4-methoxybenzyloxy)phenyl]imidazoles **7m′−o′** (0.3 mmol) in dichloromethane (3 mL), TFA (1 mL) was added and the reaction mixture was further stirred at room temperature for 2 h, It was then neutralized with saturated $NaHCO_3$ solution (25 mL), extracted with DCM (2 × 25 mL), the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

*(2-(4-Chlorophenyl)-5-(2-hydroxyphenyl)-1H-imidazol-4-yl)-(thiophen-2-yl)methanone and (2-(4-Chlorophenyl)-4-(2-hydroxyphenyl)-1H-imidazol-5-yl)(thiophen-2-yl)methanone (**7m**).* Obtained as a 50:50 inseparable mixture of tautomers, yellow solid (96.9 mg, 85%): mp 161−163 °C; R_f 0.4 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3302, 2919, 1589, 1479, 1321, 744; ^1H NMR (400 MHz, $CDCl_3$) δ 11.50 (br s, 0.5H), 11.21 (br s, 0.5H), 10.37 (br s, 0.5H), 9.58 (br s, 0.5H), 8.45 (d, J = 3.2 Hz, 0.5H), 8.04 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 4.4 Hz, 0.5H), 7.65 (d, J = 4.8 Hz, 0.5H), 7.50 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 3.6 Hz, 0.5H), 7.32 (d, J = 8.4 Hz, 1H), 7.24−7.13 (m, 2H), 7.07 (d, J = 7.6 Hz, 0.5H), 7.02 (d, J = 8.4 Hz, 0.5H), 6.97 (d, J = 8.0 Hz, 0.5H), 6.94−6.88 (m, 1H), 6.52 (t, J = 7.6 Hz, 0.5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.7, 179.0, 156.7, 155.1, 146.7, 145.8, 141.72, 141.69, 137.36, 137.35, 136.9, 136.8, 136.7, 136.4, 135.8, 135.7, 134.9, 131.6, 131.0, 129.7, 129.5, 129.2, 128.3, 127.8, 127.7, 127.2, 126.9, 126.4, 126.3, 121.8, 121.3, 119.7, 118.8, 117.5, 116.2; HRMS (ESI) m/z calcd for $C_{20}H_{14}ClN_2O_2S$ $[M + H]^+$ 381.0465 and 383.0435, found 381.0447 and 383.0423.

*(5-(2-Hydroxyphenyl)-2-(thiophen-2-yl)-1H-imidazol-4-yl)-(thiazol-2-yl)methanone and (4-(2-Hydroxyphenyl)-2-(thiophen-2-yl)-1H-imidazol-5-yl)(thiazol-2-yl)methanone (**7n**).* Obtained as a 75:25 inseparable mixture of tautomers, yellow solid (84.7 mg, 80%): mp 200−202 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3305, 2923, 1589, 1479, 1263, 821; ^1H NMR (400 MHz, DMSO-d_6) δ 13.43 (s, 0.25H), 13.36 (s, 0.75H), 9.95 (s, 0.25H), 9.80 (s, 0.75H), 8.12 (d, J = 2.4 Hz, 0.75H), 8.03 (s, 0.75H), 7.96−7.92 (m, 0.5H), 7.75 (s, 1H), 7.65 (s, 1H), 7.41 (d, J = 6.8 Hz, 0.75H), 7.26−7.18 (m, 2.25H), 6.90−6.71 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 176.4, 163.1, 155.1, 143.8, 141.2, 136.3, 135.3, 133.0, 131.3, 130.3, 128.1, 127.4, 127.3, 125.5, 118.6, 116.8, 115.6, 54.9; HRMS (ESI) m/z calcd for $C_{17}H_{12}N_3O_2S_2$ $[M + H]^+$ 354.0371, found 354.0366.

*(5-(2-Hydroxyphenyl)-2-(2-methoxyphenyl)-1H-imidazol-4-yl)-(pyridin-3-yl)methanone and (4-(2-Hydroxyphenyl)-2-(2-methoxyphenyl)-1H-imidazol-5-yl)(pyridin-3-yl)methanone (**7o**).* Obtained as a single tautomer, yellow solid (89.0 mg, 80%): mp 110−112 °C; R_f 0.3 (3:2 EtOAc/hexane); IR (neat, cm^{-1}) 3103, 1622, 1581, 1462, 1258, 750; ^1H NMR (400 MHz, DMSO-d_6) δ 10.19, (br s, 1H), 9.13 (s, 1H), 8.71 (d, J = 3.6 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 7.99 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.57 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.53−7.46 (m, 2H), 7.25−7.19 (m, 2H), 7.12 (t, J = 7.2 Hz, 1H), 6.87−6.83 (m, 2H), 3.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 185.7, 156.5, 154.7, 151.4, 149.9, 143.2, 137.8, 134.0, 131.2, 131.0, 130.3, 129.1, 123.4, 120.8, 118.7, 116.8, 116.6, 115.7, 112.0, 55.8; HRMS (ESI) m/z calcd for $C_{22}H_{18}N_3O_3$ $[M + H]^+$ 372.1348, found 372.1337.

General Procedure for Methylation and Deprotection of 7m′−o′: Synthesis of 1-(*N*-Methyl)-5-(2-hydroxyphenyl)-4-het-(aroyl)imidazoles 8m−o. To a stirred solution of imidazoles **7m′−o′** (0.3 mmol) in dry acetonitrile (3 mL), K_2CO_3 (41.4 mg, 0.3 mmol) was added and the reaction mixture was stirred at room temperature (1 h), followed by addition of MeI (0.018 mL, 0.3 mmol) and further stirring for 2h (monitored by TLC).Workup of the reaction mixture as described earlier for methylation of imidazoles **7a−k** afforded crude *N*-methylated imidazoles **8m′−o′** which were subjected to deprotection with TFA without further purification, following the similar procedure and workup as described for deprotection of **7m′−7o′**. Purification of the crude products thus obtained by column chromatography (EtOAc and hexane as eluent) afforded pure 1-*N*-methylated 4(5)-2-hydroxyphenylimidazoles **8m−o**.

*(2-(4-Chlorophenyl)-5-(2-hydroxyphenyl)-1-methyl-1H-imidazol-4-yl)(thiophen-2-yl)methanone (**8m**).* Obtained from **7m′**, yellow solid (92.1 mg, 78%): mp 128−130 °C; R_f 0.3 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3242, 1583, 1411, 1227, 835; ^1H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 2.8 Hz, 1H), 8.33 (br s, 1H), 7.72−7.70 (m, 3H), 7.52 (d, J = 8.4 Hz, 2H), 7.41 (dt, J = 8.0 Hz, 1.2 Hz, 1H), 7.24−7.15 (m, 3H), 7.06 (t, J = 7.2 Hz, 1H), 3.53 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.9, 156.8, 148.1, 142.6, 137.9, 137.6, 137.2, 136.0, 131.6, 131.3, 130.6, 129.3, 128.6, 128.2, 121.1, 121.0, 118.6, 34.4; HRMS (ESI) m/z calcd for $C_{21}H_{16}ClN_2O_2S$ $[M + H]^+$ 395.0621 and 397.0592, found 395.0615 and 397.0573.

*(5-(2-Hydroxyphenyl)-1-methyl-2-(thiophen-2-yl)-1H-imidazol-4-yl)(thiazol-2-yl)methanone (**8n**).* Obtained from **7n′**, yellow solid (97.9 mg, 89%): mp 142−144 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3244, 1612, 1463, 1277, 835; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 3.2 Hz, 1H), 7.77 (br s, 1H), 7.71 (d, J = 2.8 Hz, 1H), 7.51−7.48 (m, 2H), 7.36 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.18−7.14 (m, 3H), 7.02 (td, J = 7.6 Hz, 1.2 Hz, 1H), 3.64 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.5, 163.6, 156.3, 144.8, 143.9, 139.2, 136.7, 131.9, 131.8, 131.6, 128.2, 127.9, 127.8, 127.3, 121.1, 120.2, 117.6, 34.0; HRMS (ESI) m/z calcd for $C_{18}H_{14}N_3O_2S_2$ $[M + H]^+$ 368.0527, found 368.0515.

*(5-(2-Hydroxyphenyl)-2-(2-methoxyphenyl)-1-methyl-1H-imidazol-4-yl)(pyridin-3-yl)methanone (**8o**).* Obtained from **7o′**, yellow solid (94.7 mg, 82%): mp 65−67 °C; R_f 0.4 (7:3 EtOAc/hexane); IR (neat, cm^{-1}) 3112, 1660, 1445, 1293, 896; ^1H NMR (400 MHz, $CDCl_3$) δ 9.46 (br s, 1H), 8.68 (br s, 1H), 8.57 (d, J = 8.0 Hz, 1H), 7.54−7.48 (m, 2H), 7.41−7.35 (m, 2H), 7.23−7.19 (m, 2H), 7.10 (t, J = 7.6 Hz, 1H), 7.04−7.01 (m, 3H), 3.88 (s, 3H), 3.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.0, 157.8, 156.6, 152.7, 152.5, 147.6, 138.8, 137.9, 137.7, 132.7, 131.9, 131.60, 131.56, 123.2, 121.3, 120.9, 120.2, 119.3, 118.4, 111.2, 55.8, 33.0; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_3O_3$ $[M + H]^+$ 386.1505, found 386.1496.

One-Pot Synthesis of *N*-Propargyl/Ethylhydroxyiminoimines 14l,14p−14q from Monothioketones 1. To a stirred solution of monothio-1,3-diketone (**1g**, **1m−n**) (2.0 mmol) in dry acetonitrile (5 mL) was added appropriate α-methyleneamine (2.0 mmol) in one slot and reaction mixture was stirred at room temperature for 3 h (monitored by TLC), after complete consumption of starting materials (monitored by TLC), sodium nitrite (165.6 mg, 2.4 mmol) and acetic acid (0.17 mL, 3.0 mmol) were added and reaction mixture was further stirred at room temperature for 1 h (monitored by TLC). It was then neutralized with saturated $NaHCO_3$ solution (25 mL), extracted with EtOAc (3 × 25 mL), the combined organic layer was washed with water (3 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give crude residue which were purified by column chromatography using EtOAc/hexane as eluent.

*1-(4-Chlorophenyl)-3-(ethylimino)-2-(hydroxyimino)-3-(4-methoxyphenyl)propan-1-one (**14l**).* Obtained as a single tautomer, pale yellow solid (564.1 mg, 82%): mp 54−56 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3251, 2854, 1641, 1449, 1302, 960; ^1H NMR

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(400 MHz, DMSO-d_6) δ 13.09 (br s, 1H), 8.03 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H), 3.36−3.26 (m, 2H), 1.20 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 187.9, 161.0, 157.8, 153.3, 138.2, 134.6, 132.0, 128.5, 128.1, 114.0, 55.3, 48.2, 15.8; HRMS (ESI) m/z calcd for $C_{18}H_{18}ClN_2O_3$ $[M + H]^+$ 345.1006 and 347.0976, found 345.1003 and 347.0967.

*1-(4-Chlorophenyl)-2-(hydroxyimino)-3-(prop-2-ynylimino)-3-(thiophen-2-yl)propan-1-one (**14p**).* Obtained as a single tautomer, yellow solid (468.6 mg, 71%): mp 102−104 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3298, 2172, 1652, 1586, 1274, 718; ^1H NMR (400 MHz, DMSO-d_6) δ 13.45 (br s, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 4.8 Hz, 1H), 7.64 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 3.2 Hz, 1H), 7.07 (dd, J = 4.8 Hz, 4.0 Hz, 1H), 4.08 (qd, J = 18.4 Hz, 2.4 Hz, 2H), 3.15 (t, J = 2.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 187.4, 156.8, 151.2, 141.5, 138.2, 134.4, 132.1, 130.6, 129.7, 128.4, 127.9, 81.0, 74.2, 42.1; HRMS (ESI) m/z calcd for $C_{16}H_{12}ClN_2O_2S$ $[M + H]^+$ 331.0308 and 333.0279, found 331.0298 and 333.0263.

*3-(Benzo[d][1,3]dioxol-5-yl)-2-(hydroxyimino)-3-(prop-2-ynylimino)-1-(thiophen-2-yl)propan-1-one (**14q**).* Obtained as a single tautomer, yellow solid (496.4 mg, 73%): mp 116−118 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3298, 2160, 1652, 1422, 718; ^1H NMR (400 MHz, DMSO-d_6) δ 13.32 (br s, 1H), 8.17 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 8.15 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.31 (dd, J = 5.2 Hz, 4.0 Hz, 1H), 7.24 (d, J = 1.2 Hz, 1H), 6.96 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.08 (d, J = 1.6 Hz, 2H), 4.05 (qd, J = 18.4 Hz, 2.8 Hz, 2H), 3.13 (t, J = 2.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 179.0, 160.8, 151.9, 149.7, 148.0, 138.9, 137.3, 136.1, 129.7, 128.5, 122.2, 108.2, 105.5, 101.7, 81.3, 73.9, 42.5; HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2O_4S$ $[M + H]^+$ 341.0596, found 341.0594.

Procedure for Synthesis of 2-Ethynyl-4,5-Substituted imidazole 7p from Hydroxyiminoimine 14p. To a stirred solution of *N*-propargylhydroxyiminoimines **14p** (165.0 mg, 0.5 mmol) in dry acetonitrile (3 mL) was added K_2CO_3 (69.1 mg, 0.5 mmol) at room temperature, followed by heating at 80 °C for 3 h (monitored by TLC), the reaction mixture was treated with saturated NH_4Cl solution (25 mL), extracted with EtOAc (2 × 25 mL), the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/hexane (3:7) as eluent.

*(4-Chlorophenyl)(2-ethynyl-5-(thiophen-2-yl)-1H-imidazol-4-yl)-methanone and (4-Chlorophenyl)(2-ethynyl-4-(thiophen-2-yl)-1H-imidazol-5-yl)methanone (**7p**).* Obtained as a 80:20 inseparable mixture of tautomers, yellow solid (71.3 mg, 76%): mp 162−164 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3217, 2981, 2120, 1679, 1645, 1479, 1261, 891; ^1H NMR (400 MHz, DMSO-d_6) δ 13.89 (br s, 0.8H), 13.75 (br s, 0.2H), 8.10 (d, J = 8.4 Hz, 1.6 H), 7.94 (d, J = 8.4 Hz, 0.4 H), 7.83 (d, J = 2.8 Hz, 0.8 H), 7.73−7.70 (m, 1.2H), 7.60−7.54 (m, 2H), 7.21−7.19 (m, 0.8H), 7.01−6.99 (m, 0.2H), 4.62 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 186.1, 166.4, 137.2, 136.5, 134.6, 132.8, 132.0, 129.3, 129.0, 128.5, 128.1, 127.3, 82.7, 74.0; HRMS (ESI) m/z calcd for $C_{16}H_{10}ClN_2OS$ $[M + H]^+$ 313.0202 and 315.0173, found 313.0199 and 315.0159.

*Base Mediated Intramolecular Cyclization of α-Hydroxyiminoimine **14q**.* Attempted cyclization of hydroxyiminoimine **14q** in the presence of K_2CO_3 as described for **14p**, did not give the expected imidazole **7q**, but a different product, which could not be characterized (in the absence of single crystal X-ray data): yellow solid (58.3 mg, 60%): mp 101−103 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3273, 2127, 1658, 1598, 1449, 1235, 1065; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 4.0 Hz, 0.8 Hz, 1H), 7.61 (dd, J = 5.2 Hz, 0.8 Hz, 1H), 7.54 (d, J = 1.6 Hz, 1H), 7.46 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.00 (dd, J = 5.2 Hz, 4.0 Hz, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 2.0 Hz, 1H), 5.97 (s, 2H), 2.74 (d, J = 2.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.4, 168.5, 151.1, 148.3, 139.8, 135.4, 135.0, 128.4, 125.0, 123.4, 108.8, 108.4, 101.8, 98.9, 91.9, 78.2, 76.4; HRMS (ESI) m/z calcd for $C_{17}H_{11}N_2O_3S$ $[M + H]^+$ 323.0490 and found 324.0276.

Intramolecular Thermal Cyclization of *N*-Propargyl-α-Hydroxyiminoimines 14p−q and *N*-Propargyl-Enaminones 13p−q: Synthesis of 2,3-Substituted Pyridine 15a and 15b. A solution of either hydroxyiminoimine **14p−q** (0.3 mmol) or *N*-propargylenaminone **13p−q** (0.3 mmol) in dry DMSO (5 mL) was heated at 100 °C for 8−10 h (monitored by TLC), The reaction mixture was treated with saturated NH_4Cl solution (25 mL), extracted with EtOAc (2 × 25 mL), the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to afford crude residue which were purified by column chromatography using EtOAc/hexane as eluent.

*(4-Chlorophenyl)(2-(thiophen-2-yl)pyridin-3-yl)methanone (**15a**).* Obtained from **14p**, brown semi solid (53.2 mg, 59%): R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2921, 1664, 1578, 1437, 1274, 706; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (dd, J = 5.2 Hz, 2.0 Hz, 1H), 7.71−7.68 (m, 3H), 7.35−7.26 (m, 4H), 7.04 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 6.84 (dd, J = 5.2 Hz, 4.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.0, 150.8, 149.8, 142.6, 140.5, 136.6, 134.7, 132.4, 131.3, 129.2, 129.0, 128.8, 128.1, 121.5; HRMS (ESI) m/z calcd for $C_{16}H_{11}ClNOS$ $[M + H]^+$ 300.0250 and 302.0220, found 300.0245 and 302.0212.

*(2-(Benzo[d][1,3]dioxol-5-yl)pyridin-3-yl)(thiophen-2-yl)-methanone (**15b**).* Obtained from **14q**, pale yellow solid (60.2 mg, 65%): mp 85−87 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2896, 1644, 1501, 1405, 1230, 1046, 735; ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 7.84 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.63 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 7.34 (dd, J = 7.6 Hz, 4.8 Hz, 1H), 7.24 (dd, J = 3.6 Hz, 0.8 Hz, 1H), 7.16 (d, J = 1.6 Hz, 1H), 7.03 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 6.97 (dd, J = 4.8 Hz, 4.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.93 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.4, 156.4, 150.9, 148.5, 148.1, 144.1, 136.9, 135.4, 135.3, 134.2, 133.6, 128.3, 123.8, 121.3, 109.5, 108.4, 101.4; HRMS (ESI) m/z calcd for $C_{17}H_{12}NO_3S$ $[M + H]^+$ 310.0538, found 310.0525.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00938.

Crystallographic data for **8a** and **8d**. (CIF)

Copies of ^1H NMR and ^{13}C NMR spectra for all new compounds; X-ray crystallographic structure displays for **8a** and **8d**; three tables for optimization of reaction conditions. (PDF)

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Notes

The authors declare no competing financial interest.

■ DEDICATION

Dedicated to Professor H. Junjappa, on the occasion of his 80th birthday.

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