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TMSOTf-catalyzed synthesis of trisubstituted imidazoles using hexamethyldisilazane as a nitrogen source under neat and microwave irradiation conditions†

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In the process of drug discovery and development, an efficient and expedient synthetic method for imidazole-based small molecules from commercially available and cheap starting materials has great significance. Herein, we developed a TMSOTf-catalyzed synthesis of trisubstituted imidazoles through the reaction of 1,2-diketones and aldehydes using hexamethyldisilazane as a nitrogen source under microwave heating and solvent-free conditions. The chemical structures of representative trisubstituted imidazoles were confirmed using X-ray single-crystal diffraction analysis. This synthetic method has several advantages including the involvement of mild Lewis acid, being metal- and additive-free, wide substrate scope with good to excellent yields and short reaction time. Furthermore, we demonstrate the application of the methodology in the synthesis of biologically active imidazole-based drugs.

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Introduction

In the drug discovery and development process, obtaining small organic molecules in pure and sufficient amounts is one of the major challenges.[1] To access biologically active small molecules, the development of an efficient synthetic methodology from cheap starting materials is highly desirable.[2,3] Imidazoles, a class of nitrogen-containing five-membered ring heterocyclic compounds, have a unique chemical behavior and a broad range of biological activities.[4–6] The diverse therapeutic properties of these heterocycles include anti-inflammatory, antiproliferative, antimicrobial, anticancer, antihypertensive and inhibition of p38 MAP-kinase, angiotensin II receptor blockers and cytotoxicity.[7–13] Imidazole-based compounds have also been used as important precursors in synthesizing pharmaceuticals and natural products like alkaloids.[5,9,13–15] Some representative examples of biologically active multisubstituted imidazole drugs are shown in Fig. 1.

Trifenagrel is a type of imidazole-related drug that inhibits both arachidonate cyclooxygenase and platelet aggregation in many animal species and humans.[16,17] Fenflumizol and neurodazine are also bioactive imidazole derivatives having potential neurogenic and anti-inflammatory activities.[18,19] The tetraaryl-substituted imidazole apoptozole was reported to induce apoptosis (a programmed cell death) in murine P19 embryonic carcinoma cells and could bind to the heat shock proteins Hsp72 and Hsc70.[20,21]

The first angiotensin II receptor antagonist, losartan which is mainly used to treat high blood pressure (hypertension) and diabetic kidney disease, whereas the fused imidazole omeprazole is used as proton pump inhibitor.[20] The imidazole alkaloid, namely, lepidilines B, was isolated from the root extract of *Lepidium meyenii* and inhibits potentially cytotoxic reactions against numerous human cancer cell lines,[22] while cimetidine is a histamine H-2-receptor antagonist that inhibits gastric acid

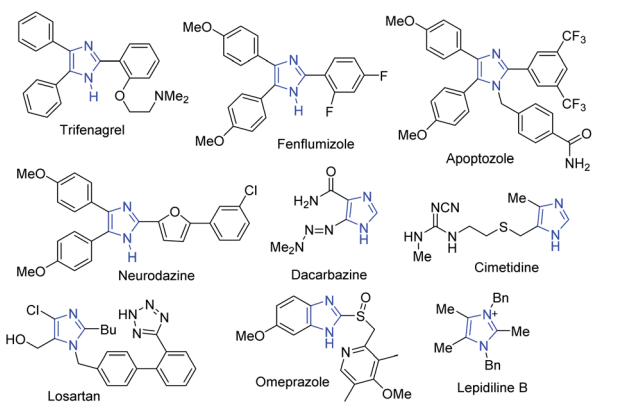

Fig. 1 Representative examples of biologically active imidazole-based drugs.

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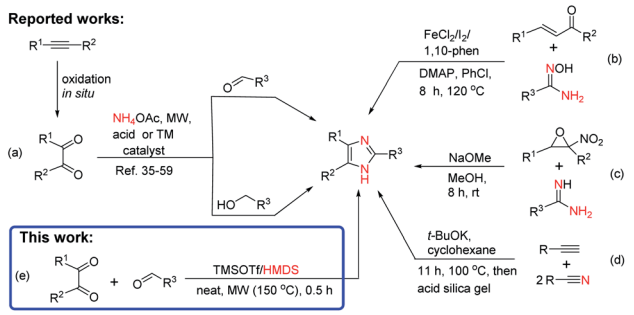
† Electronic supplementary information (ESI) available: Detailed experimental procedures and spectroscopic data for all compounds and X-ray analysis data for **3n**, **3q**, **3s**, **3w**, **4h** and **3z**. CCDC 2082023, 2082029, 2082025, 2082032, 2082036 and 2098033. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ra05802a

production.[23] Substituted imidazoles also have important applications in the chemistry of materials such as in functional polymers,[24] ligands,[25] photophysical materials,[26,27] ionic liquids,[28] semiconductor devices,[29] fluorescent probes,[30] and N-heterocyclic carbenes.[31]

Because of their versatile applications, several approaches have been developed for the chemical synthesis of imidazoles.[6,31–39] The most commonly known synthetic methods are (i) the three-component condensation reaction of benzils with -aryl aldehydes, primary alcohols, and ammonium acetate (NH_4OAc)/amines using a microwave (MW) irradiation under ionic liquid,[13] HOAc,[35,36,40,41] Fe,[42,43] Ni,[44] and Co[45] catalysis system, in the presence of acids,[6,17,36,39,46,47] urea/hydrogen peroxide (UHP),[48] organic bases,[49] carbon,[50] and transition-metal (TM) catalysts such as $TiCl_4/SiO_2$,[4] Cu[32] and Fe/Ag nanoparticles (NPs),[51] Zr NPs,[33] La/Mn NPs,[52] Au(I)[38] and Ru(II)[53,54] complexes, urea/$ZnCl_2$,[55] MoO_3/SiO_2,[56] I_2,[57] ZrO_2/Al_2O_3,[58] and sulfated SnO_2 [59] (Scheme 1a) (ii) *via* reaction of α,β-unsaturated ketones/aldehydes and internal alkynes with amidoximes using Fe(II)-catalyzed cross-dehydrogenative coupling[60] and Cs_2CO_3-promoted annulation[61] (Scheme 1b) (iii) from α-nitro-epoxides and amidines with an excess base as promoter[62] (Scheme 1c), and (iv) from base-promoted nitrile-alkyne domino-type cyclization[63] (Scheme 1d).

Although these synthetic strategies are widely established, they are performed in the presence of expensive catalysts, ligands/additives, toxic organic solvents, and under harsh reaction conditions. Owning to the fascinating and wide range of applications of multisubstituted imidazoles in biological, pharmaceutical, and material chemistry, the development of an efficient, environmentally friendly, and economic synthetic method from commercially available starting materials and mild reagents is worth considering.

Hexamethyldisilazane (HMDS), a stable and inexpensive reagent, has been used in silylation[64–67] and ring closure[68,69] reactions in the presence of protic and Lewis acid[66,68] as catalysts. In our previous work on silylation of free sugars, we found that activation of HMDS by trifluoromethanesulfonate (TMSOTf) generated gaseous ammonia (NH_3) as a byproduct,[65] making it a useful condition for the synthesis of substituted quinazolines.[68] Continuing our work on the development of an efficient synthetic methodology for the microwave-assisted synthesis of heterocycles,[68,70–72] we herein describe for the first time, TMSOTf-catalyzed solvent-free synthesis of trisubstituted imidazoles using HMDS as nitrogen source under microwave irradiation conditions (Scheme 1e).



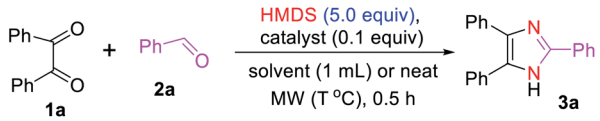
Scheme 1 Synthetic methods of 2,4,5-triisubstituted imidazoles.

Results and discussion

To optimize the reaction condition for the formation of the 2,4,5-triarylated imidazole **3a** under microwave irradiation, we selected the commercially available 1,2-diketone (**1a**, 1 equiv.) and benzaldehyde (**2a**, 2 equiv.) as model substrates using HMDS (5 equiv.) as the nitrogen source in the absence and presence of various acids as catalysts (0.1 equiv.) (Table 1). To start with, we attempted to synthesize imidazole **3a** without any catalyst. Accordingly, **3a** was formed in 18% and 16% yields in toluene and water, respectively, which was then improved to 63% when the reaction was carried out in catalyst- and solvent-free systems with microwave heating (150 °C) (Table 1, entries 1–3). This improved yield (63%) indicated that the HMDS can serve both as a reagent and a solvent.

To further prepare compound **3a** in a high yield, we conducted the reaction in the presence of Lewis acid as a catalyst. Interestingly, 84% yield of **3a** was obtained under the AgOTf catalysis system in toluene (Table 1, entry 4). Based on this promising result, we screened several Lewis acids as catalysts. A slightly higher yield of **3a** was obtained with $Cu(OTf)_2$; however, the yield dropped to 50% and 49% when $Sc(OTf)_3$ and $AlCl_3$ were employed, respectively (Table 1, entries 6 and 7) showing their low catalytic activity. Remarkably, a high yield (90%) of imidazole **3a** was achieved with protic acid (TfOH) under the same reaction condition (Table 1, entry 8).

Table 1 Optimization of the reaction conditions[a]



Entry	Catalyst	Temperature (°C)	Solvent	Yield[b] (%)
1	—	150	Toluene	18
2	—	150	Water	16
3	—	150	—	63
4	AgOTf	150	Toluene	84
5	$Cu(OTf)_2$	150	Toluene	87
6	$Sc(OTf)_3$	150	Toluene	50
7	$AlCl_3$	150	Toluene	49
8	TfOH	150	Toluene	90
9	TMSOTf	150	Toluene	Quant.
10	TMSOTf	150	DCM	93
11	TMSOTf	150	MeCN	Quant.
12	TMSOTf	150	—	96
13	TMSOTf	100	—	92
14	TMSOTf	25	—	47
15	TMSOTf	200	—	75

[a] Reaction conditions: **1a** (0.48 mmol, 1.0 equiv.), **2a** (0.95 mmol, 2.0 equiv.), HMDS (2.38 mmol, 5.0 equiv.), catalyst (0.048 mmol, 0.1 equiv.). [b] Isolated yields.

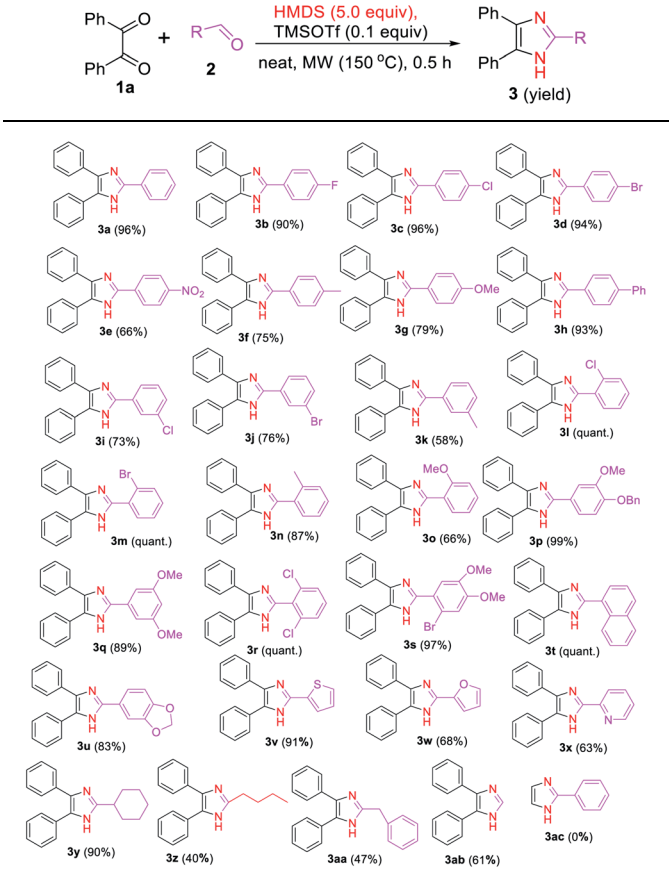
We continued to investigate the reaction conditions to obtain a better yield of imidazole **3a**. Gratifyingly, the desired product **3a** was obtained in a quantitative yield with a catalytic amount of TMSOTf under microwave heating in toluene (Table 1, entry 9). We also examined the role of dichloromethane and acetonitrile on the reaction yields that could achieve good results like that with toluene (Table 1, entries 10 and 11). Importantly, the triaryl substituted imidazole **3a** was isolated in 96% yield under solvent-free conditions (Table 1, entry 12). The yield of **3a** was not significantly affected by lowering the reaction temperature from 150 to 100 °C, but dropped to 47% when the reaction was performed at 25 °C under a neat condition (Table 1, entries 13 and 14). On the other hand, increasing the reaction temperature to 200 °C decreases the yield of imidazole **3a** (Table 1, entry 15). Indeed, the desired product **3a** was formed in excellent yields with or without solvents under the TMSOTf-catalyzed system at 150 °C. Therefore, we preferred to use the solvent-free reaction condition (Table 1, entry 12) to investigate the substrate scope based on the principles of green chemistry.[73]

We also evaluated the preparation of **3a** from **1a** and **2a** under conventional reflux heating condition, and the reaction performed well affording a comparable yield (89%) of **3a** as that of microwave-assisted reaction. Muthusubramanian and Esmaeilpour groups have also isolated similar yields of 2,4,5-trisubstituted imidazoles for reactions carried out under thermal and microwave irradiation.[43,74] It is reported that microwave-assisted organic synthesis has several advantages such as rapid homogeneous heating, suppression of side product, convenience of handling, simple work-up, short reaction time, and required less energy compared to conventional heating.[36,41–43,69,74–77] Bearing of these advantages in mind, we investigated the substrate scope under the microwave irradiation.

Next, we explored the substrate scope and generality of the imidazole formation from various substituted aryl (**2b–x**) and alkyl (**2y**, **2z**, **2aa**, **2ab**) aldehydes and benzil (**1a**) (Table 2) using the optimized reaction conditions. Thus, the aryl aldehydes having electron-withdrawing groups (**2b–e**, **2i–j**, **2l–m**, and **2r**), electron-donating substituents (**2f–h**, **2k**, and **2n–q**), and heterocycles (**2u–x**) reacted smoothly with the 1,2-diketone **1a** to provide the corresponding imidazole derivatives **3b–x** in moderate to quantitative yields. The reaction yield of **1a** with benzaldehyde derivatives bearing halides (**2b–d**) and phenyl (**2h**) groups at *para*-position was observed to be higher (90–96%) than those using aldehydes **2f–gh** and **2k** which contained activating groups (methyl and methoxy) either at the *para*- or *meta*-positions (58%, 75–79%) and deactivating substituents (**2i–j**) at *meta*-positions (73–76%). On other hand, a moderate yield (66%) of **3e** was achieved by coupling **1a** with the aryl aldehyde **2e** having a nitro group, which is a stronger deactivator than halogens.

The reaction of 1,2-diketone **1a** with aryl aldehydes **2l–m** which bear weak electron-donating effects, such as chloro, bromo, and methyl groups at *ortho*-position of the aromatic ring affords in excellent yields of imidazoles **3l–m** than those aldehydes with strong electron-rich groups, such as the methoxy

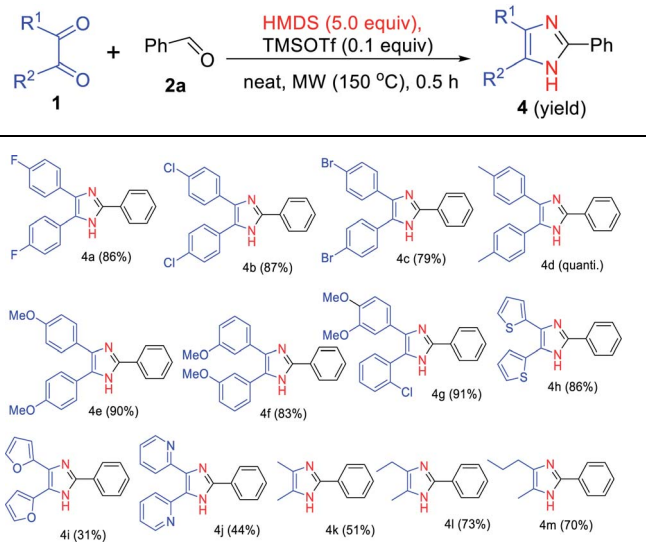
Table 2 Substrate scope of substituted aryl aldehydes **2**



group (**2o**). Similarly, multisubstituted aldehyde substrates **2p–s** with electron-donating or electron-withdrawing functionalities performed well to produce high yields of the corresponding imidazole derivatives **3p–s** ranging from 89% to quantitative under the established reaction conditions. Interestingly, high yields of trisubstituted imidazoles **3t** and **3u** were achieved by reacting **1a** with bulkier substrates **2t** and **2u** that contain fused rings, indicating that the steric effect has no influence on the formation of these imidazoles. Additionally, the scope of the reaction on heterocyclic carbaldehydes such as 2-thiophenyl **2v**, 2-furanyl **2w**, and 2-pyridyl **2x** was investigated. Hence, the condensation reaction of 2-thiophenyl **2v** with **1a** afforded a high yield (91%) of the imidazole **3v**, whereas, the reaction of aromatic aldehydes **2w** and **2x** with **1a** gave the desired products **3w** and **3x**, respectively in moderate yields (63–68%).

After adequately evaluating the scope of substituted aryl aldehydes, we examined the performance of the reaction with alkyl aldehydes such as cyclohexanecarboxaldehyde (**2y**), valeraldehyde (**2z**) and phenylacetaldehyde (**2aa**). Gratifyingly, the alky substituted aldehydes well tolerated to the established reaction conditions, providing the desired 2-alkyl-4,5-diaryl substituted imidazoles **3y–3aa** in moderate to excellent yields (40–90%) (Table 2). The yield of imidazole **3y** was significantly improved (90%) in this study compared to the literature report

Table 3 Substrate scope with respect to 1,2-diketones **1**



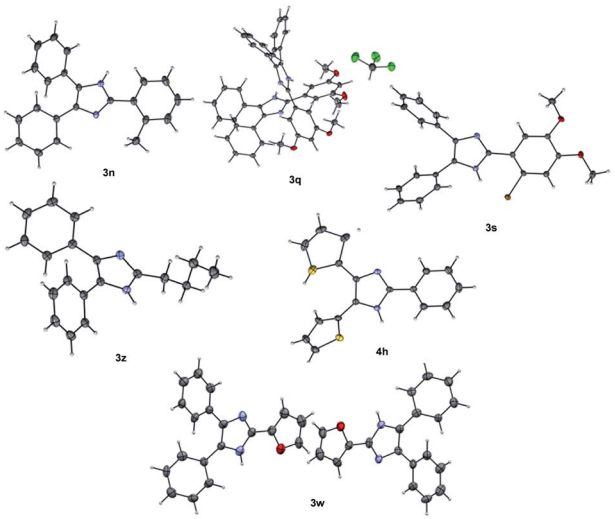
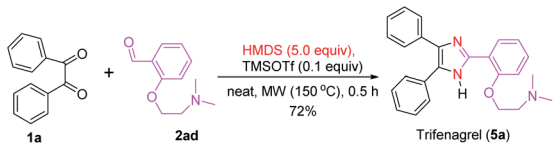


Fig. 2 Single X-ray crystal structure of **3n**, **3q**, **3s**, **3w**, **3z** and **4h**. Thermal ellipsoids was drawn at 50% probability.



Scheme 2 Synthesis of trifenagrel (**5a**).

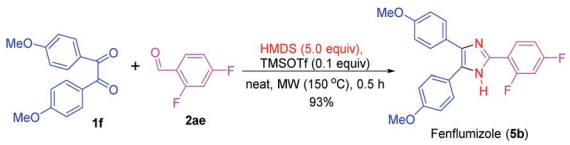
yields (18–22%) using NH_4OAc as nitrogen source.[78,79] Furthermore, the reaction was carried out on formaldehyde (**2ab**), and the corresponding 4,5-disubstituted derivative **3ab** was obtained in 61% yield. Unfortunately, the reaction of glyoxal (**2ac**) with benzaldehyde (**2a**) failed to give the desired 2-aryl substituted product **3ac**. We believe that the failure of this reaction might be attributed to the low boiling point (51 °C) of glyoxal (**2ac**) leading to its evaporation before effective reaction with benzaldehyde (**2a**).

After having screened the substrate scope of the aldehydes, we tested the condensation reaction of benzaldehyde (**2a**) with various 1,2-diketones containing electron-deficient (**1b–d**), electron-rich (**1e–g**), and heteroaromatic (**1i–l**) functional groups (Table 3). We observed that both electron-deficient (fluoro, chloro, and bromo) and electron-rich (methyl, methoxy) containing 1,2-diketones delivered very good to excellent yields (79% to quantitative) of the corresponding triaryl imidazoles **4a–f** under the established reaction condition. These results indicate that the electronic effect of the substrates has no influence on the reaction yields of **4a–f**. We also evaluated the reaction condition of unsymmetrical aryl 1,2-diketone **1h** having an electron-releasing (R^1) and electron-withdrawing group (R^2). Gratifyingly, 91% yield of the trisubstituted imidazoles **4g** was obtained by coupling of 2-chloro-3′,4′-dimethoxybenzil with **2a**. Our methodology also worked on heteroaromatic (**1i–l**) ($R^1 = R^2$ = 2-furyl, 2-thienyl and 2-pyridyl) and aliphatic 1,2-diketones **1m–o** (R^1 = Me, Et or Pr, R^2 = Me). Accordingly, the reaction of 2,2′-thenil (**1i**) and benzaldehyde (**2a**) gave a very good yield (86%) of the imidazole **4h**. However, in the case of 1,2-diketone substrates bearing O- and N-heteroatoms (**1k** and **1l**), the yield of imidazoles **4i** and **4j** decreased. The desired products **4k–m** were isolated in moderate to good yields (51–73%) through the reaction of an aliphatic 1,2-diketones **1m–o** and aldehyde **2a**.

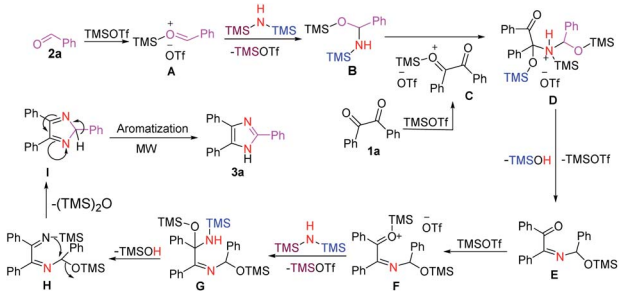
The structures of some of the trisubstituted imidazoles **3n**, **3q**, **3s**, **3w**, **3z** and **4h** were confirmed using single X-ray crystallography (Fig. 2).[80] X-ray data revealed that **3q** and **3w** are two independent isomorphous molecules.

Compared with the earlier reports, this new synthetic method for trisubstituted imidazoles has several advantages, such as the use of mild TMSOTf as a catalyst, metal- and additive-free condition, wide substrate scope with good to excellent yields and short reaction time. Moreover, the synthesis of an imidazole-based small molecule library is important for the identification of bioactive compounds that can treat several diseases.[21,81] To this end, our new synthetic methodology was applied in the synthesis of imidazole-containing drugs. Accordingly, trifenagrel (**5a**),[16,36,55] a novel potent platelet aggregation and arachidonic acid inhibitor in various animal species and humans, was synthesized in a good yield (72%) *via* the condensation of benzil (**1a**) with the aldehyde **2ad** under the optimized reaction condition (Scheme 2). This drug was previously synthesized in over two steps either from **1a** and **2ad** in the presence of catalysts and additives such as urea/$ZnCl_2$,[55] $Co(acac)_2/Ag_2O$,[82] and silica/acid[83] using NH_4OAc as nitrogen source or from the reaction 2-(4,5-diphenyl-1*H*-imidazol-2-yl) phenol and 2-bromo-*N*,*N*-dimethylethanamine under basic condition.[82,84]

This synthesis method described here was also employed in the preparation of fenflumizol (**5b**),[85] a biologically active imidazole-based drug having potential platelet aggregation and anti-inflammatory activities.[18,86] The synthesis of drug **5b** was



Scheme 3 Synthesis of fenflumizol (**5b**).



Scheme 4 Plausible mechanism for the synthesis of **3a**.

achieved by the reaction of the benzil derivative **1f** with the aromatic aldehyde **2ae** under the established reaction condition. Remarkably, this biologically active compound was obtained in 93% yield (Scheme 3). Previously, this imidazole-based natural product was synthesized from 4,4′-dimethoxybenzil (**1f**) and 2,4-diflurobenzaldehyde (**2ae**) for a longer reaction time (3 h) using NH_4OAc as the nitrogen source and acetic acid as solvent at 100 °C.[85]

Based on the experimental results in Table 1 and literature reports, we propose a plausible reaction mechanism for the formation of 2,4,5-trisubstituted imidazoles (Scheme 4). First, the carbonyl oxygen of aldehyde **2a** is activated by TMOTf to form complex **A** which then leads to a nucleophilic addition with HMDS to afford the tetrahedral intermediate **B**[87] along with the regeneration of TMOTf. Next, nucleophilic addition of the silanamine intermediate **B** to the carbonyl carbon of the activated benzil **C** produces complex **D**. A stepwise elimination of TMOTf and TMSOH from **D** gave an imine **E**, which was then followed by increasing the electrophilicity of its carbonyl group through coordination with TMOTf to furnish a complex **F**. Then the electrophilic carbonyl carbon of **F** reacts with HMDS to form the tetrahedral intermediate **G** with a concomitant recovery of TMOTf. Next, elimination of TMSOH[87] from **G** provides 1,2-diimine intermediate **H**, which in turn undergoes intramolecular cyclization to form the five-membered ring intermediate **I** upon the expulsion of $(TMS)_2O$. Finally, the desired imidazole **3a** is obtained through the aromatization of **I** under microwave irradiation. Interestingly, the formation of the ethane-1,2-diimine intermediate **H** was confirmed by mass spectrometry analysis (see ESI†).

Conclusion

We have developed a successfully and highly efficient method for the synthesis of trisubstituted imidazoles by coupling the readily available 1,2-diketones and aldehydes in the presence of TMSOTf as Lewis acid catalyst and HMDS as a nitrogen source under microwave heating and solvent-free conditions. This new synthetic method features wide substrate scope with good to excellent yields, simple starting materials, metal- and additive-free and with a short reaction time. The chemical structures of representative trisubstituted imidazoles were confirmed by X-ray single-crystal diffraction analysis. Furthermore, the potential of the methodology described here was demonstrated through the synthesis of biologically important imidazole-based drugs such as trifenagrel and fenflumizol.

Experimental section

General information

All reagents obtained from commercial sources were used without purification, unless otherwise mentioned. Column chromatography was carried out by Silica Gel Geduran® Si 60 (0.040–0.063 mm, E. Merck). TLC was performed on pre-coated glass plates of Silica Gel 60 F254 (0.25 mm, E. Merck); detection was executed by spraying with a solution of $Ce(SO_4)_2$ $(NH_4)_2MoO_4$, and H_2SO_4 in water and subsequently heating on a hot plate. UV light for TLC analysis was UVGL-25 compact UV lamp (4 watt/254 nm). Melting points were determined with a MP-2D melting apparatus. ^1H NMR, ^{13}C NMR, and DEPT spectra were recorded by Bruker DRX500 and AVIII 500. Chemical shifts are in ppm from Me_4Si, generated from the DMSO-d_6 and $CDCl_3$ lock signal at δ 2.50, 7.24 and 40.00, 77.16 ppm for ^1H and ^{13}C NMR, respectively. Multiplicities are reports by using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, s = sextet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets; J = coupling constant values in Hertz. High resolution mass spectrometry (HR-MS) was performed on a Waters Premier XE instrument with ESI source. Structural assignments were made with additional information from selective 1D-TOCSY, 2D-HSQC, 2D-HMBC and X-ray experiments.

General procedure for the synthesis of 2,4,5-trisubstituted imidazoles[68]

1,2-Diketone derivatives **1a–m** (0.272 to 1.160 mmol, 1 equiv.), aryl aldehydes **2a–ae** (2.32 to 0.543 mmol, 2 equiv.), and trimethylsilyl trifluoromethanesulfonate (0.027 to 0.116 mmol, 0.1 equiv.) in hexamethyldisilazane (1.64 to 5.81 mmol, 5 equiv.) were added into a dried 15 mL microwave vial at 25 °C. The mixture was placed in a microwave irradiation instrument and stirred at 150 °C for 0.5 h. After the reaction completion, the reaction mixture was cooled to 25 °C, dissolved in ethyl acetate and diluted with water. Next, the crude product was extracted from the aqueous phases with ethyl acetate. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in rotary vacuum to afford the crude product. Purification of the crude products by column chromatography using 3 to 15% ethyl acetate in hexane afforded the corresponding pure imidazoles **3**, **4** and **5**.

2,4,5-Triphenyl-1*H*-imidazole (3a).[4,35,46,50,55,58,75,78,82,88] White solid (135.2 mg, 96% yield); mp: 273–275 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.68 (s, 1H, NH), 8.07 (d, J = 7.9 Hz, 2H, ArH), 7.54 (d, J = 7.50 Hz, 2H, ArH), 7.50–7.42 (m, 6H, ArH), 7.38 (t, J = 6.40 Hz, 2H, ArH), 7.30 (t, J = 7.50 Hz, 2H, ArH), 7.22 (t, J = 7.20 Hz, 1H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 146.1, 137.7, 135.7, 131.6, 130.9, 129.3, 129.2, 129.0, 128.9, 128.8, 128.8, 128.4, 127.7, 127.1, 125.8; HRMS (ESI) m/z: calcd for $C_{21}H_{17}N_2$ $[M + H]^+$ 297.1386, found 297.1386.

2-(4-Fluorophenyl)-4,5-diphenyl-1*H*-imidazole (3b).[46,75,78,88] White solid (134.8 mg, 90% yield); mp: 258–260 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.70 (br s, 1H, NH), 8.14–8.10 (m, 2H, ArH), 7.53–7.30 (m, 12H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 162.6 (d, J = 245.4 Hz), 145.2, 137.6, 135.6, 131.5, 129.1, 128.9, 128.7, 128.3, 127.8 (d, J = 8.2 Hz), 127.5 (d, J = 2.7 Hz), 127.0, 116.2 (d, J = 21.7 Hz); HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2F$ $[M + H]^+$ 315.1292, found 315.1299.

2-(4-Chlorophenyl)-4,5-diphenyl-1*H*-imidazole (3c).[4,35,46,55,58,78,88] White solid (150.4 mg, 96% yield); mp: 273–275 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.78 (br s, 1H, NH), 8.10 (d, J = 8.8 Hz, 2H, ArH), 7.55–7.24 (m, 12H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 144.9, 137.8, 135.5, 133.2, 131.4, 129.7, 129.2, 129.1, 128.9, 128.7, 128.4, 127.5, 127.3, 127.1; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2Cl$ $[M + H]^+$ 331.0997, found 331.0991.

2-(4-Bromophenyl)-4,5-diphenyl-1*H*-imidazole (3d).[4,46,55,58,78,88] White solid (167.3 mg, 94% yield); mp: 265–266.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.78 (br s, 1H, NH), 8.05–8.02 (m, 2H, ArH), 7.70–7.67 (m, 2H, ArH), 7.53–7.36 (m, 10H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 144.9, 132.2, 130.0, 128.9, 127.6, 121.9; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2Br$ $[M + H]^+$ 375.0491, found 375.0498.

2-(4-Nitrophenyl)-4,5-diphenyl-1*H*-imidazole (3e).[50,54,55] Orange solid (134.8 mg, 90% yield); mp: 239–241 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 13.15 (s, 1H, NH), 8.37–8.31 (m, 4H, ArH), 7.55–7.33 (m, 10H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 147.0, 143.9, 136.6, 129.0, 127.6, 126.2, 124.8; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_3O_2$ $[M + H]^+$ 342.1237, found 342.1243.

2-(4-Methylphenyl)-4,5-diphenyl-1*H*-imidazole (3f).[4,46,58] White solid (111.2 mg, 75% yield); mp: 235–237 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.59 (br s, 1H, NH), 7.98 (d, J = 8.1 Hz, 2H, ArH), 7.55–7.22 (m, 12H, ArH), 2.35 (s, 3H, CH_3); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 146.1, 138.2, 137.4, 135.7, 131.6, 129.7, 129.1, 128.9, 128.6, 128.4, 128.2, 127.5, 126.9, 125.6, 21.4; HRMS (ESI) m/z: calcd for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1548.

2-(4-Methoxyphenyl)-4,5-diphenyl-1*H*-imidazole (3g).[4,35,46,75,78,88] White solid (123.3 mg, 79% yield); mp: 232–234 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.51 (br s, 1H, NH), 8.03–8.00 (m, 2H, ArH), 7.55–7.20 (m, 10H, ArH), 7.06–7.03 (m, 2H, ArH), 3.82 (s, 3H, OCH_3); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 159.9, 146.1, 137.2, 135.8, 131.7, 129.1, 128.8, 128.6, 128.1, 127.5, 127.2, 126.9, 123.6, 114.6, 55.7; HRMS (ESI) m/z: calcd for $C_{22}H_{19}N_2O$ $[M + H]^+$ 327.1492, found 327.1486.

2-(2-Biphenyl-4-yl)-4,5-diphenyl-1*H*-imidazole (3h).[50] White solid (164.6 mg, 93% yield); mp: 229–231 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.75 (br s, 1H, NH), 8.19 (d, J = 8.6 Hz, 2H, ArH), 7.81 (d, J = 8.5 Hz, 2H, ArH), 7.77–7.75 (m, 2H, ArH), 7.55–7.25 (m, 13H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 145.7, 140.1, 140.0, 137.8, 135.6, 131.5, 129.9, 129.5, 129.1, 128.9, 128.7, 128.3, 128.1, 127.6, 127.4, 127.2, 127.0, 126.2; HRMS (ESI) m/z: calcd for $C_{22}H_{19}N_2O$ $[M + H]^+$ 373.1699, found 373.1696.

2-(3-Chlorophenyl)-4,5-diphenyl-1*H*-imidazole (3i).[35,58] White solid (114.5 mg, 73% yield); mp: 279–281 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.82 (br s, 1H, NH), 8.15 (br s, 1H, ArH), 8.05 (d, J = 7.8 Hz, 1H, ArH), 7.56–7.22 (m, 12H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 144.5, 137.9, 135.4, 134.1, 132.8, 131.3, 131.2, 129.2, 129.2, 128.9, 128.7, 128.4, 128.4, 127.6, 127.2, 125.1, 124.2; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2Cl$ $[M + H]^+$ 331.0997, found 331.0991.

2-(3-Bromophenyl)-4,5-diphenyl-1*H*-imidazole (3j).[4,58] White solid (135.9 mg, 76% yield); mp: 270–272 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.84 (br s, 1H, NH), 8.30 (t, J = 1.7 Hz, 1H, ArH), 8.09 (dt, J = 1.3, 8.0 Hz, 1H, ArH), 7.58–7.39 (m, 9H, ArH), 7.31 (t, J = 7.4 Hz, 2H, ArH), 7.24 (t, J = 7.2 Hz, 1H, ArH); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 144.4, 137.9, 135.4, 133.0, 131.5, 131.3, 129.3, 129.2, 128.9, 128.8, 128.5, 128.0, 127.6, 127.2, 124.6, 122.7; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2Br$ $[M + H]^+$ 375.0491, found 375.0482.

4,5-Diphenyl-2-(3-methylphenyl)-1*H*-imidazole (3k).[4,58] White solid (84.8 mg, 58% yield); mp: 301–303 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.63 (br s, 1H, NH), 7.93 (br s, 1H, ArH), 7.87 (d, J = 7.8 Hz, 1H, ArH), 7.53 (dd, J = 7.4, 23.8 Hz, 4H, ArH), 7.44 (t, J = 7.4 Hz, 2H, ArH), 7.37 (q, J = 7.2, 7.6 Hz, 2H, ArH), 7.30 (t, J = 7.5 Hz, 2H, ArH), 7.21 (dd, J = 7.4, 18.0 Hz, 2H, ArH), 2.39 (s, 3H, CH_3); ^{13}C{H} NMR (125 MHz, DMSO-d_6): δ (ppm) 146.1, 138.3, 137.5, 135.7, 131.6, 130.7, 129.4, 129.1, 129.1, 128.9, 128.7, 128.6, 128.2, 127.6, 127.0, 126.2, 122.8, 21.6; HRMS (ESI) m/z: calcd for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1541.

2-(2-Chlorophenyl)-4,5-diphenyl-1*H*-imidazole (3l).[4,35,55] White solid (159.4 mg, quantitative yield); mp: 197–199 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.23 (br s, 1H, NH), 8.44 (dd, J = 1.7, 7.9 Hz, 1H, ArH), 7.67 (d, J = 7.2 Hz, 2H, ArH), 7.48–7.25 (m, 11H, ArH); ^{13}C{H} NMR (125 MHz, $CDCl_3$): δ (ppm) 143.3, 138.0, 134.7, 131.0, 130.6, 129.7, 129.7, 129.1, 128.9, 128.7, 128.5, 128.2, 128.1, 127.9, 127.8, 127.6, 127.2; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2Cl$ $[M + H]^+$ 331.0997, found 331.0988.

2-(2-Bromophenyl)-4,5-diphenyl-1*H*-imidazole (3m).[54] White solid (180.9 mg, quantitative yield); mp: 209–211 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.20 (br s, 1H, NH), 8.31 (d, J = 7.9 Hz, 1H, ArH), 7.61 (d, J = 7.3 Hz, 2H, ArH), 7.57 (d, J = 8.0 Hz, 1H, ArH), 7.42 (d, J = 7.4 Hz, 2H, ArH), 7.37–7.13 (m, 8H, ArH); ^{13}C{H} NMR (125 MHz, $CDCl_3$): δ (ppm) 144.0, 138.1, 134.7, 133.9, 131.7, 131.0, 130.2, 130.0, 129.2, 128.5, 128.2, 128.1, 127.9, 127.9, 127.7, 127.2, 119.1; HRMS (ESI) m/z: calcd for $C_{21}H_{16}N_2Br$ $[M + H]^+$ 375.0491, found 375.0487.

4,5-Diphenyl-2-(2-methylphenyl)-1*H*-imidazole (3n).[4,50] White solid (128.9 mg, 87% yield); mp: 255–257 °C; ^{1}H NMR

(500 MHz, $CDCl_3$): δ (ppm) 9.08 (br s, 1H, NH), 7.60–7.58 (m, 3H, ArH), 7.41–7.19 (m, 11H, ArH), 2.58 (s, 3H, CH_3); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 146.4, 137.8, 136.6, 134.9, 131.5, 129.9, 129.0, 128.8, 128.4, 127.9, 127.0, 126.2, 21.3; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1538.

4,5-Diphenyl-2-(2-methoxyphenyl)-1*H*-imidazole (3o).[78,88] White solid (102.6 mg, 66% yield); mp: 214–216 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.47 (br s, 1H, NH), 8.48 (dd, $J = 1.8$, 7.8 Hz, 1H, ArH), 7.68 (br s, 2H, ArH), 7.47 (br s, 2H, ArH), 7.37–7.30 (m, 7H, ArH), 7.12–7.09 (m, 1H, ArH), 7.01 (d, $J = 8.3$ Hz, 1H, ArH), 4.01 (s, 3H, OCH_3); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 159.9, 146.1, 137.7, 135.2, 131.7, 129.6, 129.0, 128.8, 128.4, 127.9, 127.7, 127.4, 127.0, 121.8, 118.3, 111.3, 56.0; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{19}N_2O$ $[M + H]^+$ 327.1492, found 327.1484.

2-(4-Benzyloxy-3-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole (3p). White solid (203.8 mg, 99% yield); mp: 223–225 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.57 (br s, 1H, NH), 7.56–7.45 (m, 6H, ArH), 7.35–7.20 (m, 11H, ArH), 6.87 (d, $J = 8.4$ Hz, 1H, ArH), 5.16 (s, 2H, OCH_2) 3.88 (s, 3H, OCH_3); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 150.2, 149.0, 146.2, 136.9, 128.7, 128.1, 128.0, 127.5, 127.4, 123.7, 117.5, 114.0, 109.6, 71.2, 56.2; HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{25}N_2O_2$ $[M + H]^+$ 433.1911, found 433.1912.

2-(3,4-Dimethoxyphenyl)-4,5-diphenyl-1*H*-imidazole (3q).[46] White solid (150.1 mg, 89% yield); mp: 240–242 °C; ^1H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.66 (br s, 1H, NH), 7.55–7.37 (m, 7H, ArH), 7.32–7.29 (m, 4H, ArH), 7.22 (t, $J = 7.1$ Hz, 1H, ArH), 6.51 (t, $J = 2.2$ Hz, 1H, ArH), 3.82 (s, 6H, OCH_3); $^{13}C\{H\}$ NMR (125 MHz, DMSO-d_6): δ (ppm) 161.2, 145.8, 137.5, 135.6, 132.6, 131.5, 129.2, 129.0, 128.8, 128.7, 128.3, 127.6, 127.0, 103.6, 103.5, 101.1, 55.8; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{21}N_2O_2$ $[M + H]^+$ 357.1598, found 357.1592.

2-(2,6-Dichlorophenyl)-4,5-diphenyl-1*H*-imidazole (3r).[55] White solid (159.4 mg, quantitative yield); mp: 236–238 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.67 (br s, 1H, NH), 7.60 (br s, 2H, ArH), 7.40–7.36 (m, 4H, ArH), 7.33–7.22 (m, 7H, ArH); $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 140.5, 136.7, 131.1, 129.9, 128.9, 128.4, 128.0; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{15}N_2Cl_2$ $[M + H]^+$ 365.0607, found 365.0599.

2-(2-Bromo-4,5-dimethoxyphenyl)-4,5-diphenyl-1*H*-imidazole (3s). White solid (201.5 mg, 97% yield); mp 235–237 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.26 (br s, 1H, NH), 7.86 (br s, 1H, ArH), 7.67 (d, $J = 7.4$ Hz, 2H, ArH), 7.47 (d, $J = 7.4$ Hz, 2H, ArH), 7.37 (d, $J = 7.1$ Hz, 2H, ArH), 7.33–7.29 (m, 3H, ArH), 7.25–7.22 (m, 1H, ArH), 7.03 (s, 1H, ArH), 3.96 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 149.9, 148.8, 144.1, 137.8, 134.7, 131.1, 129.1, 128.4, 128.0, 128.0, 127.8, 127.4, 127.2, 122.8, 116.1, 113.4, 109.6, 56.4, 56.3; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N_2O_2Br$ $[M + H]^+$ 435.0703, found 435.0706.

2-Naphthalen-1-yl-4,5-diphenyl-1*H*-imidazole (3t).[75,82] White solid (165.3 mg, quantitative yield); mp. 294.5–296 °C; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 12.80 (s, 1H, NH), 9.19 (d, $J = 8.4$ Hz, 1H, ArH), 8.01 (d, $J = 7.9$ Hz, 2H, ArH), 7.97 (dd, $J = 1.0$, 7.3 Hz, 1H, ArH), 7.65–7.57 (m, 7H, ArH); 7.45–7.26 (m, 6H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 146.0, 137.6, 135.8, 134.1, 131.5, 130.8, 129.4, 129.1, 128.7, 128.4, 128.2, 127.9, 127.7, 127.3, 127.2, 127.1, 126.6, 125.7; HRMS (ESI) *m*/*z*: calcd for $C_{25}H_{19}N_2$ $[M + H]^+$ 347.1543, found 347.1538.

2-(Benzo[*d*][1,3]dioxol-5-yl)-4,5-diphenyl-1*H*-imidazole (3u).[54,55] White solid (133.7 mg, 83% yield); mp 260–262 °C; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 12.50 (s, 1H, NH), 7.63–7.22 (m, 12H, ArH), 7.02 (d, $J = 8.5$ Hz, 1H, ArH), 6.08 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 148.1, 147.9, 145.9, 137.3, 135.7, 131.6, 129.1, 128.8, 128.7, 128.2, 127.6, 127.0, 125.1, 119.8, 109.0.106.0, 101.8; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{17}N_2O_2$ $[M + H]^+$ 341.1285, found 341.1286.

4,5-Diphenyl-2-(thiophen-2-yl)-1*H*-imidazole (3v).[54] White solid (130.9 mg, 91% yield); mp 269–271 °C; ^1H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.79 (s, 1H, NH), 7.69 (dd, $J = 1.1$, 3.6 Hz, 1H, ArH), 7.55 (dd, $J = 1.1$, 5.0 Hz, 1H, ArH), 7.50 (d, $J = 7.2$ Hz, 4H, ArH), 7.36 (br s, 6H, ArH), 7.15 (dd, $J = 3.6$, 5.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 142.1, 134.4, 129.0, 128.4, 127.9, 126.8, 124.7; HRMS (ESI) *m*/*z*: calcd for $C_{19}H_{15}N_2S$ $[M + H]^+$ 303.0951, found 303.0943.

2-(Furan-2-yl)-4,5-diphenyl-1*H*-imidazole (3w).[78,88] White solid (92.5 mg, 68% yield); mp 245–247 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.81 (br s, 1H, NH), 7.55–7.24 (m, 11H, ArH), 6.94 (d, $J = 3.4$ Hz, 1H, ArH), 6.48 (dd, $J = 1.8$, 3.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 145.7, 142.4, 139.1, 138.5, 134.6, 130.8, 128.7, 128.0, 127.3, 112.2, 107.7; HRMS (ESI) *m*/*z*: calcd for $C_{19}H_{15}N_2O$ $[M + H]^+$ 287.1179, found 287.1175.

4,5-Diphenyl-2-(2-pyridyl)-1*H*-imidazole (3x).[35,89] White solid (89.4 mg, 63% yield); mp 191–193 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.92 (br s, 1H, NH), 8.43–8.42 (m, 1H, ArH), 8.28 (dt, $J = 1.0$, 8.0 Hz, 1H, ArH), 7.75 (td, $J = 1.7$, 15.5 Hz, 1H, ArH), 7.67 (dd, $J = 1.4$, 8.5 Hz, 2H, ArH), 7.44 (dd, $J = 1.7$, 8.1 Hz, 2H, ArH), 7.33–7.23 (m, 6H, ArH), 7.17 (ddd, $J = 1.1$, 4.9, 7.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 148.9, 148.4, 145.6, 139.3, 137.2, 134.9, 130.9, 128.9, 128.7, 128.5, 128.1, 128.0, 128.0, 127.2, 123.2, 120.2; HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{16}N_3$ $[M + H]^+$ 298.1339, found 298.1340.

2-Cyclohexyl-4,5-diphenyl-1*H*-imidazole (3y).[78] White solid (128.9 mg, 90% yield); mp 245–246 °C; ^1H NMR (500 MHz, DMSO-d_6): δ (ppm) 11.95 (br s, 1H, NH), 7.43–7.23 (m, 10H, ArH), 2.73–2.67 (m, 1H), 1.97–1.95 (m, 2H, CH_2), 1.80–1.28 (m, 2H, CH_2), 1.70–1.55 (m, 3H, CH_2), 1.39–1.23 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 152.9, 128.8, 127.9, 79.7, 37.7, 26.2, 26.1; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{23}N_2$ $[M + H]^+$ 303.1856, found 303.1849.

2-*n*-Butyl-4,5-diphenyl-1*H*-imidazole (3z). Brown paste (52.7 mg, 40% yield); ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.41–7.39 (m, 4H, ArH), 7.22–7.14 (m, 6H, ArH), 2.60 (t, $J = 7.8$ Hz, 2H, CH_2), 1.58 (p, $J = 7.4$ Hz, 2H, CH_2), 1.28–1.23 (m, 2H, CH_2), 0.80 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 148.7, 132.8, 131.9, 131.1, 129.9, 128.7, 128.1, 127.9, 127.4, 30.9, 28.2, 22.6, 13.9; HRMS (ESI) *m*/*z*: calcd for $C_{19}H_{21}N_2$ $[M + H]^+$ 277.1699, found 277.1697.

2-Benzyl-4,5-diphenyl-1*H*-imidazole (3aa).[90] White solid (69.3 mg, 47% yield); mp 251–252 °C; ^1H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.28 (br, s, 1H, NH), 7.48–7.18 (m, 15H), 4.02 (s, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 147.3, 147.3, 139.0, 136.3, 136.0, 131.9, 129.2, 129.1, 128.9, 128.6,

128.2, 127.8, 127.5, 126.8, 126.8, 34.6; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1543.

4,5-Diphenyl-1*H*-imidazole (3ab).[91] White solid (63.3 mg, 61% yield); mp 231–233 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.48 (s, 1H, NH), 7.78 (s, 1H, H-2), 7.49–7.20 (m, 10H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 136.6, 136.1, 136.0, 131.8, 129.2, 128.7, 128.3, 128.0, 127.5, 126.8, HRMS (ESI) *m*/*z*: calcd for $C_{15}H_{13}N_2$ $[M + H]^+$ 221.1073, found 221.1071.

4,5-Bis(4-fluorophenyl)-2-phenyl-1*H*-imidazole (4a).[92] White solid (116.2 mg, 86% yield); mp 271–273 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.73 (br s, 1H, NH), 8.08 (d, J = 7.4 Hz, 2H, ArH), 7.57–7.52 (m, 4H, ArH), 7.48 (t, J = 7.6 Hz, 2H, ArH), 7.38 (t, J = 7.4 Hz, 1H, ArH), 7.30 (t, J = 8.6 Hz, 2H, ArH), 7.15 (t, J = 9.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 162.9 (d, J = 245.2 Hz), 160.9 (d, J = 243.4 Hz), 146.0, 136.8, 132.0 (d, J = 2.1 Hz), 131.1 (d, J = 8.1 Hz), 130.7, 129.4 (d, J = 8.0 Hz), 129.2, 128.8, 127.9 (d, J = 2.4 Hz), 116.2 (d, J = 21.6 Hz), 115.6 (d, J = 21.3 Hz); HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{15}N_2F_2$ $[M + H]^+$ 333.1198, found 333.1193.

4,5-Bis(4-chlorophenyl)-2-phenyl-1*H*-imidazole (4b).[35] White solid (114.4 mg, 87% yield); mp 292–294 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.79 (br s, 1H, NH), 8.07 (d, J = 7.5 Hz, 2H, ArH), 7.54–7.38 (m, 11H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 146.5, 130.6, 129.2, 129.0, 125.8; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{15}N_2Cl_2$ $[M + H]^+$ 365.0607, found 365.0598.

4,5-Bis(4-bromophenyl)-2-phenyl-1*H*-imidazole (4c).[78] White solid (114.4 mg, 87% yield); mp 314–316 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.79 (br s, 1H, NH), 8.07 (dd, J = 1.3, 8.5 Hz, 2H, ArH), 7.65–7.46 (m, 10H, ArH), 7.41–7.38 (m, 1H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 146.6, 136.8, 134.6, 131.9, 130.5, 129.2, 129.0, 125.8, 121.6, 120.3; HRMS (ESI) *m*/*z*: calcd for $C_{21}H_{15}N_2Br_2$ $[M + H]^+$ 452.9597, found 452.9602.

4,5-Bis(4-methylphenyl)-2-phenyl-1*H*-imidazole (4d).[54] White solid (135.4 mg, quantitative yield); mp 275–277.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.57 (br s, 1H, NH), 8.07 (dd, J = 1.2, 8.4 Hz, 2H, ArH), 7.48–7.35 (m, 7H, ArH), 7.24 (br s, 2H, ArH), 7.12 (br s, 2H, ArH), 2.34 (br s, 3H, CH_3), 2.30 (br s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 145.6, 137.5, 137.4, 136.0, 132.9, 130.9, 129.6, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.3, 127.5, 125.6, 21.3; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{21}N_2$ $[M + H]^+$ 325.1699, found 325.1691.

4,5-Bis(4-methoxyphenyl)-2-phenyl-1*H*-imidazole (4e).[93] White solid (119.0 mg, 90% yield); mp 200–202 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.83 (dd, J = 1.5, 8.5 Hz, 2H, ArH), 7.40–7.33 (m, 6H, ArH), 7.31–7.28 (m, 1H, ArH), 6.82 (d, J = 8.7 Hz, 4H, ArH), 3.78 (s, 6H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 159.0, 145.7, 130.2, 129.2, 128.9, 128.6, 125.4, 114.1, 55.4; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{21}N_2O_2$ $[M + H]^+$ 357.1598, found 357.1589.

4,5-Bis(3-methoxyphenyl)-2-phenyl-1*H*-imidazole (4f). White solid (109.2 mg, 83% yield); mp 196–197.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.98 (br s, 1H, NH), 7.85 (d, J = 7.6 Hz, 2H, ArH), 7.38–7.30 (m, 3H, ArH), 7.18 (t, J = 7.8 Hz, 2H, ArH), 7.07 (br s, 4H, ArH), 6.79 (d, J = 7.3 Hz, 2H, ArH), 3.68 (s, 6H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.7, 146.1, 130.0, 129.6, 129.0, 128.9, 125.5, 120.5, 113.7, 113.1, 55.3; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{21}N_2O_2$ $[M + H]^+$ 357.1598, found 357.1590.

5-(2-Chlorophenyl)-4-(3,4-dimethoxyphenyl)-2-phenyl-1*H*-imidazole (4g). White solid (117.2 mg, 91% yield); mp 205–207 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.81 (br s, 1H, NH), 7.85 (d, J = 6.7 Hz, 2H, ArH), 7.38 (d, J = 7.9 Hz, 1H, ArH), 7.31–7.27 (m, 4H, ArH), 7.21 (td, J = 1.6, 15.5 Hz, 1H, ArH), 7.14 (td, J = 0.9, 15.0 Hz, 1H, ArH), 6.91 (d, J = 7.4 Hz, 2H, ArH), 6.65 (d, J = 8.4 Hz, 1H, ArH), 3.75 (s, 3H, OCH_3), 3.50 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 148.6, 148.0, 146.2, 134.2, 132.7, 130.0, 129.9, 129.5, 128.8, 128.7, 126.9, 125.6, 119.1, 111.1, 110.1, 55.8, 55.4; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{20}N_2O_2Cl$ $[M + H]^+$ 391.1208, found 391.1199.

4,5-Di(thiophen-2-yl)-2-phenyl-1*H*-imidazole (4h). White solid (119.0 mg, 86% yield); mp 269–271 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.87 (br s, 1H, NH), 8.05–8.03 (m, 2H, ArH), 7.71 (d, J = 4.6 Hz, 1H, ArH), 7.50–7.47 (m, 2H, ArH), 7.43–7.38 (m, 3H, ArH), 7.22 (dd, J = 3.6, 5.0 Hz, 1H, ArH), 7.17 (d, J = 3.0 Hz, 1H, ArH), 7.02 (dd, J = 3.7, 4.9 Hz, 1H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ (ppm) 148.2, 137.9, 134.1, 131.2, 130.2, 129.2, 129.1, 129.0, 128.1, 127.9, 127.8, 125.8, 125.3, 123.9, 121.2; HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{13}N_2S_2$ $[M + H]^+$ 309.0515, found 309.0513.

4,5-Di(furan-2-yl)-2-phenyl-1*H*-imidazole (4i).[94] Brown solid (45.1 mg, 31% yield); mp 192–194 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.89 (dd, J = 1.4, 8.5 Hz, 2H, ArH), 7.47 (d, J = 0.9 Hz, 2H, ArH), 7.42–7.39 (m, 2H, ArH), 7.37–7.34 (m, 1H, ArH), 6.95 (br s, 2H, ArH), 6.50 (dd, J = 1.8, 3.3 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 146.3, 141.6, 129.4, 129.3, 129.0, 125.6, 111.9, 110.1, 107.7; HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{13}N_2O_2$ $[M + H]^+$ 277.0972, found 277.0971.

4,5-Di(pyrid-2-yl)-2-phenyl-1*H*-imidazole (4j).[95] Pale yellow solid (61.6 mg, 44% yield); mp 181–183 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 11.24 (br s, 1H, NH), 8.58 (br s, 3H, ArH), 8.19–8.13 (m, 1H, ArH), 7.98 (dd, J = 1.5, 8.5 Hz, 2H, ArH), 7.77–7.67 (m, 2H, ArH), 7.43–7.40 (m, 2H, ArH), 7.37–7.33 (m, 1H, ArH), 7.18 (br s, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 148.6, 146.3, 136.8, 129.7, 129.2, 129.0, 125.7, 122.3; HRMS (ESI) *m*/*z*: calcd for $C_{19}H_{14}N_4Na$ $[M + Na]^+$ 321.1111, found 321.1109.

4,5-Dimethyl-2-phenyl-1*H*-imidazole (4k).[35] Pale yellow solid (73.7 mg, 52% yield); mp 171–173 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.81 (dd, J = 1.3, 8.5 Hz, 2H, ArH), 7.36–7.33 (m, 2H, ArH), 7.05 (d, J = 7.2 Hz, 1H), 2.19 (s, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 144.1, 131.3, 130.5, 128.9, 128.0, 124.8, 11.9; HRMS (ESI) *m*/*z*: calcd for $C_{11}H_{13}N_2$ $[M + H]^+$ 173.1073, found 173.1069.

4-Ethyl-5-methyl-2-phenyl-1*H*-imidazole (4l).[96] Pale yellow solid (135.8 mg, 73% yield); mp 151–153 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.76 (dd, J = 1.4, 8.6 Hz, 2H, ArH), 7.33 (t, J = 7.2 Hz, 2H, ArH), 7.26 (dt, J = 1.1, 7.3 Hz, 1H, ArH), 2.56 (q, J = 7.6 Hz, 2H, CH_2), 2.19 (s, 3H, CH_3), 1.19 (t, J = 7.5 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 144.1, 130.7, 128.9, 128.1, 124.9, 14.6; HRMS (ESI) *m*/*z*: calcd for $C_{11}H_{13}N_2$ $[M + H]^+$ 187.1230, found 187.1225.

5-Methyl-4-propyl-2-phenyl-1*H*-imidazole (4m). Yellow sticky paste (123.2 mg, 70% yield); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.82 (dd, J = 1.4, 8.6 Hz, 2H, ArH), 7.29 (t, J = 7.2 Hz, 2H, ArH), 7.24–7.20 (m, 1H, ArH), 2.47 (t, J = 7.5 Hz, 2H, CH_2), 2.15 (s, 3H,

CH_3), 1.55 (s, $J = 7.4$ Hz, 2H, CH_2), 0.85 (t, $J = 7.4$ Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 144.3, 130.7, 128.8, 127.9, 124.9, 27.5, 23.4, 13.9, 11.2; HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{17}N_2$ $[M + H]^+$ 201.1386, found 201.1388.

2-(2-(4,5-Diphenyl-1*H*-imidazol-2-yl)phenoxy)-*N*,*N*-dimethylethanamine (5a).[36,55,82,84] White solid (131.1 mg, 72% yield); mp: 115–116.5 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.45 (dd, $J =$ 1.7, 7.8 Hz, 1H, ArH), 7.56 (br s, 4H, ArH), 7.31–7.24 (m, 7H, ArH), 7.10 (td, $J = 1.0$, 15.2 Hz, 1H, ArH), 7.00 (dd, $J = 0.6$, 8.2 Hz, 1H, ArH), 4.21 (t, $J = 5.2$ Hz, 2H, OCH_2), 2.65 (t, $J =$ 5.2 Hz, 2H, NCH_2), 1.96 (s, 6H, CH_3); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 155.2, 143.9, 129.2, 129.0, 128.5, 122.3, 120.4, 113.8, 65.8, 58.2, 44.6; HRMS (ESI) *m*/*z*: calcd for $C_{25}H_{25}N_3O$ $[M + H]^+$ 384.2070, found 384.2063.

4,5-Bis(4-methoxyphenyl)-2-(2,4-difluorophenyl)-1*H*-imidazole (5b).[85] White solid (131.1 mg, 72% yield); mp: 58–60 °C; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.56 (s, 1H, NH), 8.38–8.33 (m, 1H, ArH), 7.53–7.38 (m, 4H, ArH), 6.99 (td, $J = 2.3$, 10.2 Hz, 1H, ArH), 6.93–6.88 (m, 5H, ArH), 3.81 (s, 6H, OCH_3); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 163.7 (d, $J = 12.7$ Hz), 161.7 (d, $J =$ 12.7 Hz), 160.4 (d, $J = 11.8$ Hz), 159.5, 159.4, 158.9, 158.5 (d, $J =$ 11.7 Hz), 140.0, 130.1 (dd, $J = 4.9$, 9.4 Hz), 129.1, 114.4 (dd, $J =$ 3.3, 10.6 Hz), 114.0, 112.7 (d, $J = 21.4$ Hz), 104.3 (t, $J = 26.2$ Hz), 55.4; HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{19}N_2O_2F_2$ $[M + H]^+$ 393.1409, found 393.1403.

Author contributions

The manuscript has been prepared with contributions from all the authors.

Conflicts of interest

The authors declare no competing financial interest.

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