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Imidazoles from nitroallylic acetates and α -bromonitroalkenes with amidines: synthesis and trypanocidal activity studies

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Cascade reactions of amidines with nitroallylic acetates and α -bromonitroalkenes provide potentially bioactive imidazoles in good to excellent yields in most cases. While 2,4-disubstituted imidazol-5-yl acetates are formed in the first case, 2,4-disubstituted imidazoles, bearing no substituent at position 5, are the products in the second case. These two series of imidazoles, viz. 2,4,5-trisubstituted and 2,4-disubstituted, were screened for their activity against protozoan parasite *Trypanosoma cruzi* which is responsible for Chagas disease. As many as three compounds were as active as the standard benznidazole and two others were 2-3-fold more active highlighting the potential of substituted imidazoles, easily accessible from nitroalkenes, as possible anti-parasitic agents.

Introduction

Several imidazole containing compounds exhibit activity against *Trypanosoma cruzi*, a parasite that causes Chagas disease.¹ Synthesis and detailed evaluation of such anti-parasitic activity of imidazoles, including studies on their mechanism of action, have been reported in recent literature.² Other biological properties of imidazoles and their applications for the treatment of various diseases have also been well documented (Figure 1).³ The presence of imidazoles in bioactive compounds, including natural products,⁴ for instance, marine alkaloids,⁵ received considerable attention. Potential applications of imidazoles in coordination chemistry⁶ and as precursors to ionic liquids⁷ and stable carbenes⁸ are also noteworthy.

Many new multi-component⁹ and metal-mediated¹⁰⁻¹² approaches have appeared in the literature for the synthesis of imidazoles. However, the three component reaction of 1,2-dicarbonyl compound, aldehyde and ammonia,¹³ and the reaction of (α -halo)ketones or diketones with formamide/amines¹⁴ or amidines¹⁵ are the classical ones. Reaction of amidines with acetylenes¹¹ and nitroalkenes¹² also lead to substituted imidazoles.

In essence, functionalized and fused imidazoles are attractive targets for synthetic chemists due to their diverse applications in chemistry and biology.¹⁶

From another perspective, the reactivity of conjugated nitroalkenes as substrates in reactions as diverse as Michael addition, Diels-Alder reaction, 1,3-dipolar cycloaddition and Morita-Baylis-Hillman reaction has been amply demonstrated.¹⁷ In particular, the Morita-Baylis-Hillman (MBH)¹⁸ reactions of nitroalkenes has emerged as a convenient means to synthesize α -functionalized nitroalkenes which could in turn serve as excellent substrates for the synthesis of complex molecules.¹⁹⁻²² Several carbocycles²⁰ and heterocycles²¹⁻²² have been synthesized exploiting the 1,2 or 1,3-bi-electrophilic character of the nitroallylic acetates through a cascade S_N2 or S_N2' reaction of a binucleophile followed by an intramolecular Michael addition.

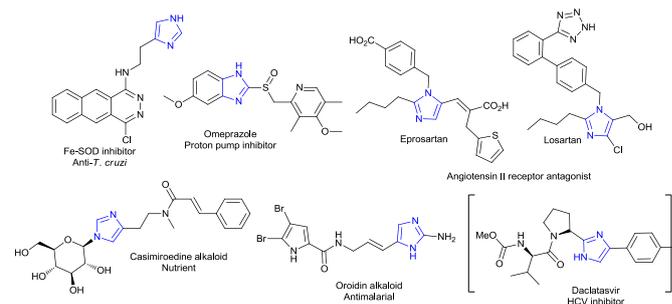


Figure 1 Selected examples of bioactive imidazoles

Among nitroalkenes, α -bromonitroalkenes, by virtue of their 1,2-bielectrophilic character, are capable of taking part in cascade reactions with various binucleophiles. Their reaction with 1,3-dicarbonyl compounds,²³ enamines,²⁴ and other miscellaneous binucleophiles²⁵ provided various functionalized heterocycles such as furans, pyrroles, pyrazoles, triazoles among others. However, to our knowledge, there is no report on the reaction of α -bromonitroalkenes with amidines for the synthesis of functionalized imidazoles.

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This work describes the full version of our studies on the synthesis of imidazoles by treating amidines with nitroallylic acetates and α -bromonitroalkenes and studies on their trypanocidal activity.²⁶

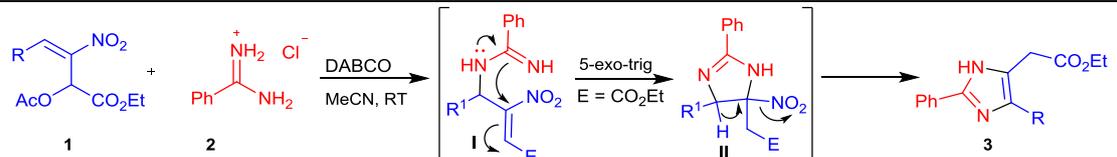
Results and discussion

In our recent communication,²⁶ we reported the synthesis of imidazole esters **3** from nitroallylic acetates **1** and amidines **2** through a one-pot cascade intermolecular aza-S_N2' reaction-intramolecular aza-Michael addition (Table 1). Selected imidazole esters **3** were transformed to alcohols **4**, acids **5** and then to amides **6** (Scheme 1). Many of these imidazoles were screened for their activity against the protozoan parasite *T. cruzi*, the etiological agent of Chagas disease. In particular, the

activity of imidazole esters **3a** and **3b** was comparable to that of the standard benzimidazole. More importantly, imidazole ester **3e** exhibited activity twice that of benzimidazole thus prompting us to synthesize and screen more imidazoles in this series and also those with other substitution pattern.

At the outset, imidazoles **3h**, **3o**, **3p** (Table 1, entries 8, 15-16) and **4d**, **5a**, **5d**, **6a** and **6d** (Scheme 1) which were reported in our previous communication,²⁶ but could not be screened earlier were later evaluated for their activity. Unfortunately, none of them yielded positive results. While **3h**, **3o** and **3p** showed activity approximately half (IC₅₀/24 h in the range of 190-214 μ M) of that of the standard, benzimidazole (IC₅₀/24h 103.6 μ M), the other derivatives **4d**, **5a**, **5d**, **6a** and **6d** did not show any activity at all (IC₅₀/24h > 300 μ M).

Table 1 Synthesis of imidazoles **3** from nitroallylic acetates **1** and amidines **2** and their activity against *T. cruzi* trypomastigotes

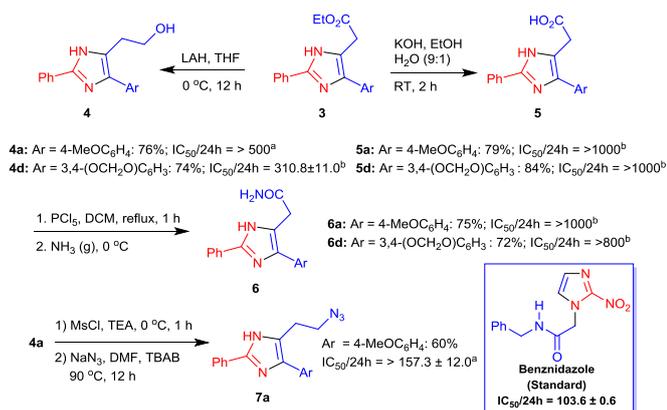


Entry	1, R ¹	2, R ²	Time (h)	3	% Yield ^a	IC ₅₀ /24 h (μ M) ^{b,c}
1	1a , 4-MeOC ₆ H ₄	C ₆ H ₅	3	3a	92	111.9 \pm 15.4
2	1b , 2,4-(MeO) ₂ C ₆ H ₃	C ₆ H ₅	4	3b	68	102.0 \pm 10.3
3	1c , 3,4-(MeO) ₂ C ₆ H ₃	C ₆ H ₅	3	3c	86	236.2 \pm 16.4
4	1d , 5-Benzo[d][1,3]dioxole	C ₆ H ₅	2	3d	91	193.0 \pm 08.6
5	1e , 4-MeC ₆ H ₄	C ₆ H ₅	3	3e	91	51.1 \pm 04.3
6	1f , C ₆ H ₅	C ₆ H ₅	4	3f	89	561.7 \pm 56.6
7	1g , 4-FC ₆ H ₄	C ₆ H ₅	2	3g	68	256.6 \pm 21.9
8	1h , 4-ClC ₆ H ₄	C ₆ H ₅	0.5	3h	67	213.9 \pm 22.8 ^d
9	1i , 3-BrC ₆ H ₄	C ₆ H ₅	0.5	3i	65	187.5 \pm 05.5
10	1j , 1-Naphthyl	C ₆ H ₅	4	3j	67	190.8 \pm 02.3
11	1k , 2-Furyl	C ₆ H ₅	7	3k	74	1002.6 \pm 76.8
12	1l , 2-Thienyl	C ₆ H ₅	2	3l	62	734.9 \pm 41.8
13	1m , C ₆ H ₅ CH=CH	C ₆ H ₅	1.5	3m	58	382.2 \pm 46.7
14	1n , Cyclohexyl	C ₆ H ₅	1	3n	67	172.0 \pm 00.8
15	1o , C ₆ H ₅	4-MeC ₆ H ₄	2	3o	69	192.7 \pm 21.6 ^d
16	1p , C ₆ H ₅	4-ClC ₆ H ₄	1.5	3p	54	194.5 \pm 14.4 ^d
17	1q , C ₆ H ₅	3-ClC ₆ H ₄	1	3q	88	221.2 \pm 28.2
18	1r , C ₆ H ₅	CH ₃	1	3r	62	946.7 \pm 12.2
19	1s , C ₆ H ₅	CH ₃ S	1.5	3s	32	1402.3 \pm 260
20	1t , 3,4-(MeO) ₂ C ₆ H ₃	4-ClC ₆ H ₄	2.5	3t	63	>600 ^e
21	1u , 3,4-(MeO) ₂ C ₆ H ₃	3-ClC ₆ H ₄	1	3u	67	>600 ^e
22	1v , 3,4-(MeO) ₂ C ₆ H ₃	4-MeC ₆ H ₄	2.5	3v	63	>1000 ^e

^a After purification by column chromatography. ^b Mean \pm SD of at least 3 independent experiments. ^c Positive control: benzimidazole IC₅₀ 103.6 \pm 0.6. ^d IC₅₀/24h was not reported in ref 26. ^e New compound

In view of the above, imidazole esters **3t-v** were synthesized following the general procedure reported by us earlier (Table 1, entries 20-22). Additionally, imidazole ester **3a** was transformed to alcohol **4a** using LAH in 76% yield and the alcohol **4a**, in turn, was converted to azide **5a** in 60% yield (Scheme 1). Subsequently, esters **3t-v**, alcohol **4a** and azide **5a** were subjected to trypanocidal activity studies as before. However, while esters **3t-v** and alcohol **4a** were inactive, azide

7a showed only moderate activity (IC₅₀/24h 157.3 μ M). It is worth mentioning the potential of the clickable imidazole **7a** that can be considered as an important intermediate in click chemistry reactions for the synthesis of hybrids compounds.



Scheme 1 Synthesis of derivatives of selected imidazole esters **3a** and **3d** and their activity against *T. cruzi* trypanosomes (^a New compound. ^b IC₅₀/24 h was not reported in ref 26). IC₅₀/24h reported in μM.

In the above scenario, we decided to explore the possibility of synthesizing imidazoles with different substitution pattern by our own methodology and screen them for their trypanocidal activity. Interestingly, although synthesis of imidazoles of type **9** via various miscellaneous methods is known in the literature,^{27–36} the reaction of amidines **2** with α-bromonitroalkenes **8** has not been employed for such purpose. At the outset, amidine **2a** and α-bromonitroalkene **8a** were chosen as model substrates in order to establish the optimal conditions (Table 2).

Table 2 Optimization studies for the synthesis of imidazole **9a** from α-bromonitroalkene **8a** and amidine **2a**

Entry	Base (equiv)	Solvent	Time (h)	% Yield ^a
1	Cs ₂ CO ₃ (1)	THF	24	- ^b
2	Cs ₂ CO ₃ (2)	THF	18	55
3	Cs ₂ CO ₃ (3)	THF	12	85
4	K ₂ CO ₃ (3)	THF	12	80
5	DMAP (3)	THF	12	56
6	DABCO (3)	THF	12	61
7	NEt ₃ (3)	THF	12	49
8	Cs ₂ CO ₃ (3)	CH ₃ CN	3	93
9	Cs ₂ CO ₃ (3)	Toluene	5	75

^a After silica gel column chromatography. ^b No reaction.

There was no appreciable conversion when 1 equiv of Cs₂CO₃ was employed as base in THF at room temperature even after 24 h (entry 1). However, upon increasing the loading of Cs₂CO₃ to 2 and 3 equiv, there was dramatic rise in the product yields to 55% and 85% as well as improvement in the reaction rate to 18 h and 12 h, respectively (entries 2–3). While K₂CO₃ also gave comparable yields (80%) of the product **9a** (entry 4), amine bases such as DMAP, DABCO and Et₃N were less effective (entries 5–7) under otherwise identical conditions. Finally, change of solvent to CH₃CN enabled us to improve the yield further to 93% and considerably reduce the reaction time to 3 h (entry 8) though the yield was much lower (75%) in a hydrocarbon solvent such as toluene (entry 9).

Table 3 Synthesis of imidazoles **8** from α-bromonitroalkenes **7** and amidine **2a**

Entry	8	R	Time (h)	9	% Yield ^a	IC ₅₀ /24h (μM) ^{b,c}
1	8a	4-MeOC ₆ H ₄	3.0	9a	93	177.2 ± 20.7
2	8b	3,4-(MeO) ₂ C ₆ H ₄	3.0	9b	92	372.5 ± 29.9
3	8c	5-Benzo[d][1,3]dioxole	3.0	9c	90	194.5 ± 14.2
4	8d	C ₆ H ₅	3.0	9d	88	377.2 ± 37.6
5	8e	4-MeC ₆ H ₄	3.0	9e	92	240.6 ± 32.9
6	8f	4-MeSC ₆ H ₄	6.0	9f	84	256.2 ± 9.8
7	8g	4-ClC ₆ H ₄	4.5	9g	86	332.2 ± 41.9
8	8h	4-FC ₆ H ₄	4.5	9h	76	329.8 ± 33.1
9	8i	3-BrC ₆ H ₄	4.0	9i	74	339.4 ± 16.5
10	8j	2-O ₂ NC ₆ H ₄	5.0	9j	85	395.2 ± 5.3
11	8k	2-Thienyl	4.5	9k	85	352.1 ± 16.5
12	8l	3-Thienyl	5.0	9l	71	355.3 ± 3.0
13	8m	1-Naphthyl	5.5	9m	81	35.5 ± 4.3
14	8n	C ₆ H ₅ CH=CH	6.0	9n	67	157.8 ± 23.6
15	8o	Cyclohexyl	5.0	9o	85	99.6 ± 5.2
16	8p	<i>n</i> -Butyl	5.0	9p	75	151.1 ± 3.2

^a After silica gel column chromatography. ^b Mean ± SD of at least 3 independent experiments. ^c Positive control: benzimidazole IC₅₀ 103.6 ± 0.6.

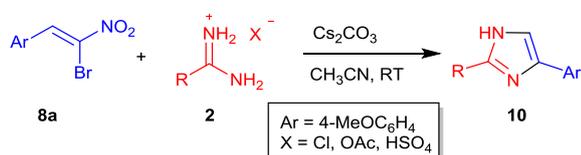
The above optimized conditions were successfully employed for the synthesis of a variety of 2,5-disubstituted imidazoles **9**-

10 (Tables 3–4). Initially, benzimidine **2a** was treated with bromonitroalkenes **8** bearing various substituents at the β-

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position to afford imidazoles **9** (Table 3). In particular, bromonitroalkenes bearing electron rich aryl groups at the β -position **8a-c** and **8e** provided the products **9a-c** and **9e**, respectively, in excellent yield (>90%, entries 1-3 and 5). The only exception among nitroalkenes bearing electron rich aryl group was **8f** which afforded the product **9f** in slightly lower yield (84%) and longer reaction time (6 h, entry 6). The yields of imidazoles derived from nitroalkenes bearing parent phenyl **8d**, electron deficient aryls **8g-j** and a fused aryl **8m** at the β -position were in the range of 74-88% (entries 4, 7-10 and 13). Heteroaryl substituted bromonitroalkenes **8k-l** also delivered the corresponding imidazoles **9k-l** in good to high yield (71-85%, entries 11-12). While bromonitroalkene **8n** afforded the product **9n** in moderate yield (67%, entry 14), β -alkylated nitroalkenes **8o-p** were better substrates and provided the desired imidazoles **9o-p** in 75-85% yield (entries 15-16).

Table 4 Synthesis of imidazoles **10** from α -bromonitroalkene **8a** and amidines **2**



Entry	2	R	Time (h)	10	% Yield ^a	IC ₅₀ /24h (μM) ^{b,c}
1	2b	4-MeC ₆ H ₄	3.5	10b	87	123.0 ± 13.9
2	2c	4-ClC ₆ H ₄	4.0	10c	79	182.6 ± 16.5
3	2d	3-ClC ₆ H ₄	3.5	10d	83	184.4 ± 7.1
4	2e	MeS	5.0	10e	55	213.8 ± 14.6
5	2f	NH ₂	2.0	10f	- ^d	-
6	2g	H	3.0	10g	- ^d	-

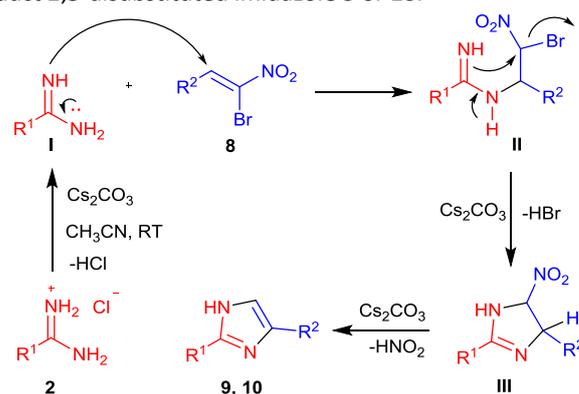
^a After silica gel column chromatography. ^b Mean ± SD of at least 3 independent experiments. ^c Positive control: benznidazole IC₅₀ 103.6 ± 0.6. ^d Complex mixture.

Having demonstrated the wide scope of bromonitroalkenes **8** in the reaction with amidine **2a**, the scope of amidines **2** was investigated by taking bromonitroalkene **8a** as the representative substrate (Table 4). The reaction of **8a** proceeded well with various arylamidines **2b-d** to afford the products **10b-d** in high yield (79-87%, entries 1-3). However, lower yield of imidazole **10e** was encountered with thioamidine **2e** (55%, entry 4). Guanidine **2f** and formamidine **2g** were not suitable substrates for the synthesis of imidazoles **10f-g** as complex mixtures were isolated under our experimental conditions (entries 5-6).

The structure and regiochemistry of imidazoles **9** and **10** were confirmed by comparison of their spectral data with those reported in the literature. In the proposed mechanism, the free amidine **I** derived from neutralization of amidinium hydrochloride **2** by base adds to bromonitroalkene **8** in a Michael fashion to afford intermediate **II**. Intramolecular nucleophilic substitution of bromide in **II** in a 5-exo-tet fashion provides the cyclized intermediate nitroimidazoline **III** which

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then undergoes base mediated elimination of HNO₂ to give the product 2,5-disubstituted imidazole **9** or **10**.



Scheme 2 Possible mechanism for formation of imidazoles **9-10** via [3+2] cycloaddition of amidines **2** with bromonitroalkenes **8**.

Trypanocidal activity studies

In the case of imidazoles **3-7** derived from nitroallylic acetates **1**, the most active compound was imidazole ester **3e** (2-fold more potent than current drug benznidazole) followed by esters **3b** and then **3a**, presenting IC₅₀/24h values of 51.1, 102.0 and 111.9 μM, respectively. These three imidazoles possess a phenyl group at position 2 and an aryl group at position 5 bearing weakly or strongly electron donating substituent(s) at *ortho/para* position(s). Presence of groups such as CH₂CO₂H, CH₂CONH₂, CH₂CH₂OH, CH₂CH₂N₃ at position 5 did not improve the activity as compared to CH₂CO₂Et (Scheme 1 and Table 1). This was also a motivating factor to synthesize imidazoles of type **9-10** wherein there is no substituent at position 5. Evaluation of the IC₅₀ values of imidazoles **9-10** in Tables 3-4 reveal that imidazole **9m** bearing a phenyl group at position 2 and a naphthyl group at position 4 is 3-fold more active (IC₅₀/24h = 35.5 μM, Table 3, entry 13) than the standard benznidazole. This is followed by **9o** with a phenyl group at position 2 and a cyclohexyl group at position 4 (IC₅₀/24h = 99.6 μM, Table 3, entry 15) which is as active as benznidazole. Imidazole **10b** with a *p*-tolyl group at position 2 and a *p*-anisyl group at position 4 (IC₅₀/24 h = 123.0 μM, Table 4, entry 1) is marginally less active than benznidazole. Other analogs which show appreciable activity which is attributable to substituents at positions 2 and 4 are **9p** (Ph, *n*-Bu, IC₅₀/24 h = 151.1 μM, Table 3, entry 16), **9n** (Ph, styrenyl, IC₅₀/24 h = 157.8 μM, Table 3, entry 14), **9a** (Ph, *p*-anisyl, IC₅₀/24 h = 177.2 μM, Table 3, entry 1), **10c** (*p*-anisyl, *p*-ClC₆H₄, IC₅₀/24 h = 182.6 μM, Table 4, entry 2), **10d** (*p*-anisyl, *m*-ClC₆H₄, IC₅₀/24 h = 184.4 μM, Table 4, entry 3) and **9c** (Ph, benzo[d][1,3]dioxole, IC₅₀/24 h 194.5 μM, Table 3, entry 3).

In general, our compounds possess low molecular weight, partition coefficient and polar surface area values adhering to the Lipinski's rules. For the compounds described herein, the hydrophobicity appears sufficient for penetrating the biological membranes of the parasite, as determined by Lipinski rule of 5 (clogP < 5, molecular weight ≤ 500, and PSA ≤ 140 Å², number of hydrogen bond acceptors < 10 and donors <

5).³⁷ Finally, a chemical informatics approach³⁸ was used to calculate the octanol-water partition coefficient (clog P value) and molecular polar surface area (PSA) for the most active compounds **3a**, **3b**, **3e**, **9m**, **9o** and **10b**, with IC₅₀/24h in the range of 35.5 to 123 μ M. The clog P and PSA values were in the range of 4.16-4.87 and 28.68-73.46, respectively.

Conclusions

Substituted imidazoles have been synthesized using amidines via a cascade S_N2'-intramolecular aza-Michael addition-elimination with nitroallylic acetates and via a cascade Michael addition-intramolecular S_N2 reaction with α -bromonitroalkenes. Imidazoles belonging to both the series have been screened against *T. cruzi* bloodstream trypomastigotes, an infective form of the protozoa that causes Chagas disease. While three of the imidazoles exhibited activity comparable to the effect of the standard compound benznidazole, the activity of two others were two- and three-fold that of the current drug, suggesting possible application of such imidazoles as effective anti-*T. cruzi* agents.

Experimental section

General. The melting points recorded are uncorrected. NMR spectra (¹H, ¹H decoupled ¹³C, ¹³C-APT and ¹H-¹H COSY) were recorded with TMS as the internal standard. The coupling constants (J values) are given in Hz. High resolution mass spectra were recorded under ESI Q-TOF conditions. Amidinium salt **2a** was purchased from Sigma-Aldrich and others **2b-d** were prepared following published procedures.³⁶ The MBH alcohols and their acetates **1** were prepared by reported procedures.³⁹ Bromonitroalkenes **8** were prepared by literature methods.⁴⁰ Experimental data for compounds **3a-s**, **4d**, **5a**, **5d**, **6a**, **6d** and **7a** were reported in our preliminary communication.²⁶

Trypanocidal Assay. Stock solutions of the compounds were prepared in dimethyl sulfoxide (DMSO), with the final concentration of the latter in the experiments never exceeding 0.4%. Preliminary experiments showed that DMSO has no deleterious effect on the parasites when its concentration is up to 4%. *T. cruzi* bloodstream trypomastigotes (Y strain) were obtained at the peak of parasitaemia from infected albino mice, purified by differential centrifugation and resuspended in RPMI to a parasite concentration of 10⁷ cells/mL in the presence of 10% of mouse blood. This suspension (100 μ L) was added in the same volume of each compound previously prepared at twice the desired final concentrations for 24h at 4°C. Cell quantification were performed in Neubauer chamber and the trypanocidal activity was expressed as IC₅₀/24h, corresponding to the concentration that leads to lysis of 50% of the parasites. The activity of standard benznidazole was reported earlier.⁴¹ It is different from that reported by Moraes et al⁴² due to different experimental conditions.

General procedure for the synthesis of imidazoles from nitroallylic acetates. To a stirred solution of amidine **2** (0.24 mmol) and DABCO (61 mg, 0.5 mmol) in acetonitrile (2 mL),

MBH acetate **1** (0.2 mmol) was added. After the completion of reaction, monitored by TLC, the solvent was removed *in vacuo* and the crude product was purified by silica gel column chromatography by gradient elution with pet ether/ethyl acetate (20-70%).

Ethyl 2-(2-(4-chlorophenyl)-4-(3,4-dimethoxyphenyl)-1H-imidazol-5-yl)acetate (3t). Yellow solid; 63%, 50 mg; mp 128- $^{\circ}$ C; IR (KBr, cm⁻¹) 2963 (m), 2934 (m), 1730 (vs), 1667 (m), 1613 (m), 1593 (m), 1510 (vs), 1481 (s), 1465 (s), 1442 (s), 1254 (vs), 1228 (s), 1176 (s), 1143 (s), 1093 (m), 1027 (vs), 836 (m), 811 (m), 765 (m), 736 (vs); ¹H NMR (CDCl₃, 400 MHz) δ 7.75 (d, J = 8.6 Hz, 2H), 7.30 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 1.8 Hz, 1H), 6.99 (dd, J = 8.3, 1.8 Hz, 1H), 6.84 (d, J = 8.3 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.87 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 171.6, 149.1, 148.6, 144.7, 134.5, 129.0, 128.3, 126.7, 124.7, 119.8, 111.3, 110.9, 61.6, 56.0, 55.9, 32.7, 14.3; MS (ES⁺, Ar) m/z (rel intensity) 403 ([MH+2]⁺, 33), 401 (M⁺, 100), 248 (15), 110 (25); HRMS (ES⁺) calcd for C₂₁H₂₂ClN₂O₄ (MH⁺) 401.1263, found 401.1269.

Ethyl 2-(2-(3-chlorophenyl)-4-(3,4-dimethoxyphenyl)-1H-imidazol-5-yl)acetate (3u). Yellow solid; yield 67%, 54 mg; mp 126 $^{\circ}$ C; IR (KBr, cm⁻¹) 2961 (w), 2935 (w), 2838 (w), 1732 (s), 1593 (m), 1510 (s), 1465 (s), 1453 (m), 1320 (w), 1254 (vs), 1227 (s), 1175 (s), 1142 (s), 1026 (s), 865 (w), 737 (vs); ¹H NMR (CDCl₃, 400 MHz) δ 7.78 (s, 1H), 7.67 (td, J = 4.4, 1.6 Hz, 1H), 7.23-7.26 (m, 2H), 7.11 (d, J = 1.6 Hz, 1H), 6.98 (dd, J = 8.3, 1.6 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.78 (s, 2H), 1.26 (t, J = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 171.6, 149.1, 148.6, 144.3, 134.9, 131.5, 130.2, 128.7, 125.4, 123.5, 119.8, 111.3, 110.8, 61.7, 56.0, 56.0, 32.7, 14.3; MS (ES⁺, Ar) m/z (rel intensity) 403 ([MH+2]⁺, 33), 401 (MH⁺, 100), HRMS (ES⁺) calcd for C₂₁H₂₂ClN₂O₄ (MH⁺) 401.1263, found 401.1261.

Ethyl 2-(4-(3,4-dimethoxyphenyl)-2-p-tolyl-1H-imidazol-5-yl)acetate (3v). Light yellow liquid; yield 63%, 48 mg; IR (neat, cm⁻¹) 2957 (m), 2925 (m), 2853 (w), 1732 (vs), 1614 (m), 1596 (m), 1514 (s), 1464 (m), 1300 (m), 1255 (vs), 1229 (s), 1174 (m), 1142 (m), 1026 (vs), 825 (m), 733 (m); ¹H NMR (CDCl₃, 400 MHz) δ 7.74 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 1.9 Hz, 1H), 7.17 (d, J = 8.2 Hz, 2H), 7.04 (dd, J = 8.3, 1.9 Hz, 1H), 6.87 (d, J = 8.3 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.78 (s, 2H), 2.34 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 171.5, 149.2, 148.5, 145.9, 138.8, 129.7, 127.2, 125.4, 119.8, 111.4, 111.0, 61.5, 56.1, 56.0, 32.5, 21.5, 14.3; MS (ES⁺, Ar) m/z (rel intensity) 381 (MH⁺, 100), 349 (5), 320 (10), 301 (8); HRMS (ES⁺) calcd for C₂₂H₂₅N₂O₄ (MH⁺) 381.1809, found 381.1810.

2-(4-(4-Methoxyphenyl)-2-phenyl-1H-imidazol-5-yl)ethan-1-ol (4a). To a stirred suspension of LAH (16 mg, 0.4 mmol) in THF (3 mL) at 0 $^{\circ}$ C, was added slowly a solution of ester **3** (70 mg, 0.2 mmol) in THF (1 mL). The reaction mixture was allowed to warm to ambient temperature and stirred for an additional 12 h. After the completion of the reaction (monitored by TLC), saturated solution of NH₄Cl (5 mL) was added, the resulting mixture was filtered through a pad of celite and the filtrate was concentrated. To the aqueous layer was added ethyl acetate (10 mL), the layers were separated and the organic

phase was washed with brine (3 × 5 mL) and water (3 × 5 mL) and dried over anhyd Na₂SO₄. The combined organic layers were concentrated in vacuo and the residue was subjected to silica gel column chromatography (72% EtOAc/pet ether). Colorless solid; yield 45 mg, 76%; mp 196–198 °C; IR (KBr, cm⁻¹) 3397 (br vs), 2925 (w), 1613 (m), 1508 (s), 1463 (m), 1248 (vs), 1177 (m), 1032 (s), 831 (w), 757 (w), 696 (w); ¹H NMR (CDCl₃ + MeOH 3:1, 400 MHz) δ 7.78 (d, *J* = 7.9 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 2H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.23–7.27 (m, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 3.75–3.75 (m, 2H), 3.74 (s, 3H), 2.87 (t, *J* = 6.5 Hz, 2H); ¹³C NMR (CDCl₃ + MeOH 3:1, 100 MHz) δ 158.9, 145.2, 133.0, 130.0, 129.4, 128.8 (× 2), 125.4, 124.6, 114.1, 61.8, 55.3, 28.9; MS (ES⁺, Ar) *m/z* (rel intensity) 317 (MNa⁺, 50), 295 (MH⁺, 100); HRMS (ES⁺) calcd for C₁₈H₁₉N₂O₂ (MH⁺) 295.1441, found 295.1441.

5-(2-Azidoethyl)-4-(4-methoxyphenyl)-2-phenyl-1H-imidazole (7a). To a stirred solution of imidazolyl alcohol **4a** (147 mg, 0.5 mmol) in dry CH₂Cl₂ (10 mL) triethylamine (0.21 mL, 152 mg, 1.5 mmol, 3 equiv) was added at 0 °C, followed by mesyl chloride (0.12 mL, 172 mg, 1.5 mmol, 3 equiv). The resulting reaction mixture was stirred for 1 h at 0 °C and then for an additional 2 h at room temperature. After the completion of reaction, the reaction mixture was diluted with water (10 mL), extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic layers were thoroughly washed with water (3 × 10 mL) to remove the excess mesyl chloride followed by saturated NaHCO₃ (3 × 10 mL) and 5% dil HCl (3 × 10 mL). The organic layer was dried over anhyd Na₂SO₄ and concentrated in vacuo. The crude mesylate was suspended in DMF (8 mL) to which NaN₃ (130 mg, 2 mmol, 4 equiv) was added followed by TBAB (16 mg, 0.05 mmol, 10 mol%). Then the reaction mixture was heated at 90 °C for 12 h. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were concentrated in vacuo and the residue was purified by silica gel column chromatography to afford diazide **7a** as colorless oil; yield 60%, 95 mg; IR (neat, cm⁻¹) 2933 (br m), 2101 (m), 1616 (w), 1507 (s), 1462 (m), 1286 (m), 1250 (vs), 1177 (m), 1029 (w), 912 (w), 835 (m), 735 (m); ¹H NMR (CDCl₃ + MeOH, 500 MHz) δ 7.83 (d, *J* = 7.7 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 2H), 7.29–7.36 (m, 3H), 6.90 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 3.52 (t, *J* = 7.0 Hz, 2H), 2.92 (t, *J* = 7.0 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 159.1, 145.9, 130.2, 128.9 (× 2), 128.7, 125.4, 114.3, 55.5, 51.1, 26.7; MS (ES⁺, Ar) *m/z* (rel intensity) 320 (MH⁺, 100); HRMS (ES⁺) calcd for C₁₈H₁₈N₅O (MH⁺) 320.1506, found 320.1515.

General Procedure for the Synthesis of Imidazoles 9-10 from α-bromonitroalkenes **8 and amidines **2**.** To a stirred solution of α-bromonitroalkene **8** (0.2 mmol) in CH₃CN (3 mL), was added benzamidinium hydrochloride **2** (0.2 mmol) followed by Cs₂CO₃ (195 mg, 0.6 mmol) at room temperature. The stirring was continued at room temperature and the completion of the reaction was monitored by TLC analysis. The crude reaction mixture was directly subjected silica gel column chromatography by eluting with 15–50% EtOAc-pet ether (gradient elution).

4-(4-Methoxyphenyl)-2-phenyl-1H-imidazole (9a).²⁷ White solid; Yield 93%, 47 mg; mp 175–177 °C (lit²⁷ 178–179 °C); IR

(KBr, cm⁻¹) 3161 (w), 2928 (w), 2836 (w), 1607 (w), 1500 (s), 1462 (w), 1249 (vs), 1180 (m), 1030 (m), 835 (m), 694 (m); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.02 (d, *J* = 7.1 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.59 (s, 1H), 7.47–7.45 (m, 2H), 7.37–7.35 (m, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 3.77 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 158.9, 147.2, 138.6, 130.1, 128.9, 128.7, 126.5, 125.7, 125.3, 117.3, 114.3, 55.4; MS (ES⁺, Ar) *m/z* (rel intensity) 273 (MNa⁺, 14), 251 (MH⁺, 100), 132 (10); HRMS (ES⁺, Ar) calcd for C₁₆H₁₅N₂O (MH⁺) 251.1179, found 251.1180. The experimental data are consistent with those reported in the literature.²⁷

4-(3,4-Dimethoxyphenyl)-2-phenyl-1H-imidazole (9b).²⁸ Off white solid; Yield 92%, 52 mg; mp 89–91 °C; IR (neat, cm⁻¹) 3320 (w), 2933 (w), 2837 (w), 1591 (w), 1528 (w), 1506 (vs), 1464 (m), 1252 (vs), 1223 (m), 1142 (m), 1025 (s), 856 (w), 765 (w); ¹H NMR (400 MHz, CDCl₃) δ 7.87 (dd, *J* = 8.4, 2.8 Hz, 2H), 7.35 (s, 1H), 7.21–7.28 (m, 5H), 6.81 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H), 3.72 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 149.1, 148.2, 147.4, 138.9, 130.2, 128.8, 128.7, 125.8, 125.7, 117.7, 117.5, 111.6, 108.7, 55.9, 55.7; MS (ES⁺, Ar) *m/z* (rel intensity) 303 (MNa⁺, 08), 282 (14), 281 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₇H₁₇N₂O₂ (MH⁺) 281.1285, found 281.1287. Reported only in patent literature.²⁸ No experimental data are available.

4-(Benzo[d][1,3]dioxol-5-yl)-2-phenyl-1H-imidazole (9c).²⁸ White solid; Yield 90%, 48 mg; mp 156–158 °C; IR (KBr, cm⁻¹) 3402 (br, m), 2892 (w), 1644 (m), 1486 (s), 1233 (vs), 1111 (w), 1039 (s), 936 (w); ¹H NMR (500 MHz, CD₃CN) δ 7.94 (d, *J* = 7.5 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.39–7.37 (m, 2H), 7.35–7.32 (m, 2H), 6.88 (d, *J* = 8.4 Hz, 1H), 5.98 (s, 2H); ¹³C NMR (126 MHz, CD₃CN) δ 149.1, 147.6, 147.4, 140.8, 131.5, 129.8, 129.4, 129.2, 126.2, 119.2, 116.5, 109.4, 106.3, 102.3; MS (ES⁺, Ar) *m/z* (rel intensity) 287 (MNa⁺, 08), 265 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₆H₁₃N₂O₂ (MH⁺) 265.0972, found 265.0973. Reported only in patent literature.²⁸ No experimental data are available.

2,4-Diphenyl-1H-imidazole (9d).^{27a} White solid; Yield 88%, 39 mg; mp 275–277 °C (lit^{27a} 274–275 °C); IR (KBr, cm⁻¹) 3378 (vs), 2923 (vw), 1640 (s), 1490 (vw), 1460 (vw), 1020 (w), 756 (w), 693 (w); ¹H NMR (400 MHz, CDCl₃) δ 9.30 (br s, 1H), 7.79–7.84 (m, 2H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.35–7.31 (m, 2H), 7.21–7.29 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 147.6, 138.9, 132.4, 129.8, 129.0, 128.9, 128.8, 127.3, 125.8, 125.2, 118.0; MS (ES⁺, Ar) *m/z* (rel intensity) 243 (MNa⁺, 31), 221 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₅H₁₃N₂ (MH⁺) 221.1073, found 221.1080. The experimental data are consistent with those reported in the literature.^{27a}

2-Phenyl-4-(*p*-tolyl)-1H-imidazole (9e).²⁹ White solid; Yield 92%, 43 mg; mp 156–159 °C; IR (KBr, cm⁻¹) 3190 (vs), 2920 (m), 2855 (m), 1729 (m), 1661 (w), 1607 (w), 1501 (m), 1460 (s), 1265 (m), 1139 (m), 1020 (w), 953 (w), 821 (s), 775 (s), 694 (s); ¹H NMR (500 MHz, DMSO-*d*₆) δ 12.60 (br s, 1H), 8.03 (d, *J* = 7.0 Hz, 2H), 7.75 (d, *J* = 7.0 Hz, 2H), 7.65 (s, 1H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.35 (t, *J* = 7.1 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 2H), 2.31 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 146.1, 139.7, 135.7, 131.0, 130.7, 129.3, 128.9, 128.3, 125.1, 124.6, 116.2, 20.9; MS (ES⁺, Ar) *m/z* (rel intensity) 235 (MH⁺, 100), 121 (3); HRMS (ES⁺, Ar) calcd for C₁₆H₁₅N₂ (MH⁺) 235.1230, found 235.1231. No experimental data are available.²⁹

4-(4-(Methylthio)phenyl)-2-phenyl-1H-imidazole (9f).³⁰ White solid; Yield 84%, 45 mg; mp 158-160 °C; IR (KBr, cm^{-1}) 3145 (br, vs), 2916 (br m), 1681 (br m), 1604 (m), 1489 (vs), 1460 (s), 1411 (m), 1297 (w), 1105 (m), 953 (m), 824 (m), 775 (m), 708 (s), 693 (s); ^1H NMR (500 MHz, DMSO-d_6) δ 12.65 (br s, 1H), 8.04 (d, $J = 6.9$ Hz, 2H), 7.82 (d, $J = 7.4$ Hz, 2H), 7.71 (s, 1H), 7.48 (t, $J = 6.9$ Hz, 2H), 7.38 (d, $J = 6.9$ Hz, 1H), 7.30 (d, $J = 7.4$ Hz, 2H), 2.50 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 146.0, 135.6, 130.6, 128.7, 128.1, 126.3, 124.9, 15.0; MS (ES^+ , Ar) m/z (rel intensity) 289 (MNa^+ , 87), 267 (MH^+ , 100); HRMS (ES^+ , Ar) calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{S}$ (MH^+) 267.0950, found 267.0950.

4-(4-Chlorophenyl)-2-phenyl-1H-imidazole (9g).²⁷ White solid; Yield 86%, 44 mg; mp 273-275 °C (lit²⁷ 277-280 °C); IR (KBr, cm^{-1}) 3413 (m), 2923 (w), 2852 (w), 1643 (m), 1488 (vs), 1461 (s), 1412 (w), 1265 (m), 1092 (m), 833 (s), 776 (m), 693 (m); ^1H NMR (400 MHz, CDCl_3) δ 8.58 (br s, 1H), 7.75-7.85 (m, 2H), 7.61 (d, $J = 7.2$ Hz, 2H), 7.40-7.20 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.9, 139.3, 138.9, 132.7, 131.5, 129.9, 129.1, 129.0, 126.4, 125.8, 117.1; MS (ES^+ , Ar) m/z (rel intensity) 257 (36), 256 (19), 255 (MH^+ , 100); HRMS (ES^+ , Ar) calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{Cl}$ (MH^+) 255.0684, found 255.0683. The experimental data are consistent with those reported in the literature.²⁷

4-(4-Fluorophenyl)-2-phenyl-1H-imidazole (9h).³¹ Pale pink solid; Yield 76%, 36 mg; mp 163-165 °C (lit³¹ 167-168 °C); IR (KBr, cm^{-1}) 3412 (br w), 3069 (br s), 2807 (br m), 1607 (vw), 1497 (s), 1462 (m), 1296 (w), 1231 (s), 1156 (m), 1083 (w), 954 (w), 838 (m), 774 (m), 693 (m); ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.86 (m, 2H), 7.70 (dd, $J = 7.7, 5.6$ Hz, 2H), 7.33-7.38 (m, 3H), 7.26 (s, 1H), 7.05 (t, $J = 8.5$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.2 (d, $J = 246.5$ Hz), 147.5, 139.3, 130.0, 129.2 (d, $J = 3.0$ Hz), 129.1, 129.0, 126.9 (d, $J = 8.0$ Hz), 125.7, 116.1, 115.7 (d, $J = 21.1$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ -119.2; MS (ES^+ , Ar) m/z (rel intensity) 261 (MNa^+ , 7), 240 ($[\text{M}+2]^+$, 15), 239 (MH^+ , 100); HRMS (ES^+ , Ar) calcd for $\text{C}_{15}\text{H}_{12}\text{FN}_2$ (MH^+) 239.0979, found 239.0979. The experimental data are consistent with those reported in the literature.³¹

4-(3-Bromophenyl)-2-phenyl-1H-imidazole (9i). Greenish liquid; Yield 74%, 44 mg; IR (neat, cm^{-1}) 3063 (br m), 2961 (br m), 2834 (br m), 1604 (w), 1493 (s), 1464 (m), 1247 (vs), 1179 (m), 1080 (w), 1031 (m), 834 (m), 768 (m); ^1H NMR (500 MHz, DMSO-d_6) δ 12.77 (br s, 1H), 8.08 (s, 1H), 8.02 (d, $J = 6.4$ Hz, 2H), 7.85-7.90 (m, 2H), 7.48 (t, $J = 5.9$ Hz, 2H), 7.42-7.32 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 146.4, 139.5, 137.1, 130.6, 130.4, 128.8, 128.7, 128.3, 126.8, 125.1, 123.3, 122.1, 115.4; MS (ES^+ , Ar) m/z (rel intensity) 301 ($[\text{M}+2]^+$, 98), 299 (MH^+ , 100), 251 (53), 185 (25), 153 (29), 129 (47); HRMS (ES^+ , Ar) calcd for $\text{C}_{15}\text{H}_{12}\text{BrN}_2$ (MH^+) 299.0178, found 299.0191.

4-(2-Nitrophenyl)-2-phenyl-1H-imidazole (9j).³² Yellow solid; Yield 85%, 45 mg; mp 157-159 °C; IR (KBr, cm^{-1}) 3247 (br s), 1612 (vw), 1526 (vs), 1485 (w), 1460 (w), 1366 (s), 1093 (br w), 780 (m), 748 (w), 694 (m); ^1H NMR (500 MHz, CDCl_3) δ 10.18 (br s, 1H), 7.93-7.89 (unresolved m, 1H), 7.83 (d, $J = 7.7$ Hz, 2H), 7.72 (br d, $J = 6.7$ Hz, 1H), 7.58 (t, $J = 7.7$ Hz, 1H), 7.43-7.36 (m, 4H), 7.31 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.2, 146.3, 136.3, 131.6, 130.2, 129.2, 128.8, 128.5, 127.5, 127.1, 125.0, 123.3, 116.6; MS (ES^+ , Ar) m/z (rel intensity) 288 (MNa^+ , 54), 267 ($[\text{M}+2]^+$, 15), 266 (MH^+ , 100); HRMS (ES^+ , Ar) calcd for

$\text{C}_{15}\text{H}_{12}\text{N}_3\text{O}_2$ (MH^+) 266.0924, found 266.0926. Reported only in patent literature.³² No experimental data are available.

2-Phenyl-4-(thiophen-2-yl)-1H-imidazole (9k).³³ Greenish liquid; Yield 85%, 38 mg; IR (neat, cm^{-1}) 3067 (br, m), 2894 (m), 1606 (vw), 1486 (vs), 1343 (vw), 1234 (vs), 1110 (w), 1039 (s), 935 (m), 813 (m), 775 (m), 695 (m); ^1H NMR (500 MHz, CDCl_3) δ 7.85-7.75 (unresolved m, 2H), 7.35-7.27 (unresolved m, 4H), 7.26 (s, 1H), 7.20-7.17 (m, 1H), 7.04-7.00 (unresolved m, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 147.5, 136.4, 135.2, 129.9, 129.0, 129.0, 127.8, 125.8, 123.8, 122.8, 116.4; MS (ES^+ , Ar) m/z (rel intensity) 249 (MNa^+ , 100), 235 (14), 227 (8); HRMS (ES^+ , Ar) calcd for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{SNa}$ (MNa^+) 249.0457, found 249.0456. Experimental data are not available in the literature.

2-Phenyl-4-(thiophen-3-yl)-1H-imidazole (9l).³⁴ Off white solid; Yield 71%, 32 mg; mp 146-148 °C (lit³⁴ 151-153 °C); IR (KBr, cm^{-1}) 3067 (br, vs), 2911 (m), 1459 (m), 1423 (m), 1404 (m), 1267 (w), 1212 (w), 1137 (m), 1031 (w), 846 (m), 775 (m), 693 (vs), 667 (m); ^1H NMR (500 MHz, CDCl_3) δ 7.87 (d, $J = 7.3$ Hz, 2H), 7.67 (s, 1H), 7.48-7.43 (m, 3H), 7.39 (t, $J = 7.3$ Hz, 1H), 7.30 (d, $J = 5.7$ Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 145.3, 134.5, 134.2, 130.0, 128.7, 128.4, 128.2, 127.0, 125.2, 117.2, 105.2; MS (ES^+ , Ar) m/z (rel intensity) 249 (MNa^+ , 9), 241 (13), 227 (MH^+ , 100), 139 (4); HRMS (ES^+ , Ar) calcd for $\text{C}_{13}\text{H}_{11}\text{N}_2\text{S}$ (MH^+) 227.0637, found 227.0637. Only mp and CHN data are reported in the literature.³⁴

4-(Naphthalen-1-yl)-2-phenyl-1H-imidazole (9m). Off white solid; Yield 81%, 44 mg; mp 159-161 °C; IR (KBr, cm^{-1}) 3063 (br, vs), 2918 (s), 1499 (m), 1461 (s), 1414 (w), 1265 (m), 1142 (w), 954 (w), 822 (s), 775 (m), 737 (m), 693 (s); ^1H NMR (500 MHz, CDCl_3) δ 8.34-8.32 (m, 1H), 7.90-7.87 (m, 3H), 7.82 (d, $J = 8.2$ Hz, 1H), 7.62 (d, $J = 7.7$ Hz, 1H), 7.53-7.45 (m, 3H), 7.40-7.38 (m, 2H), 7.36-7.33 (m, 1H), 7.31 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 145.8, 138.2, 133.7, 130.9, 130.7, 130.3, 128.9, 128.4, 128.3, 127.5, 126.3, 126.2, 126.1, 125.8, 125.6, 125.2, 119.8; MS (ES^+ , Ar) m/z (rel intensity) 309 (MK^+ , 26), 293 (MNa^+ , 72), 271 (MH^+ , 100); HRMS (ES^+ , Ar) calcd for $\text{C}_{19}\text{H}_{15}\text{N}_2$ (MH^+) 271.1230, found 271.1225.

(E)-2-Phenyl-4-styryl-1H-imidazole (9n). Yellow oily liquid; Yield 67%, 33 mg; IR (neat, cm^{-1}) 3203 (br, m), 3066 (m), 2954 (vs), 2926 (vs), 1600 (w), 1485 (m), 1463 (s), 1378 (vw), 1248 (s), 1026 (w), 754 (s), 706 (m); ^1H NMR (500 MHz, CDCl_3) δ 8.81 (br s, 1H), 7.92 (d, $J = 6.6$ Hz, 2H), 7.33 (d, $J = 7.5$ Hz, 2H), 7.33-7.25 (m, 5H), 7.16-7.23 (m, 2H), 7.11, 6.98 (ABq, $J = 16.4$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 147.9, 137.4, 136.1, 129.9, 129.0, 129.0, 128.8, 127.5, 127.5, 126.3, 125.9, 122.7, 117.7; MS (ES^+ , Ar) m/z (rel intensity) 269 (MNa^+ , 20), 247 (MH^+ , 100); HRMS (ES^+ , Ar) calcd for $\text{C}_{17}\text{H}_{15}\text{N}_2$ (MH^+) 247.1230, found 247.1230.

4-Cyclohexyl-2-phenyl-1H-imidazole (9o).³⁵ Colorless liquid; Yield 85%, 38 mg; IR (neat, cm^{-1}) 3401 (br, m), 2925 (s), 2852 (m), 1644 (w), 1463 (w), 1412 (w), 1266 (w), 1092 (w), 773 (w), 709 (w), 694 (w); ^1H NMR (500 MHz, CDCl_3) δ 7.84-7.82 (m, 2H), 7.32-7.25 (m, 3H), 6.78 (s, 1H), 2.62-2.55 (m, 1H), 2.04-1.97 (m, 2H), 1.78-1.72 (m, 2H), 1.71-1.64 (m, 1H), 1.42-1.16 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.7, 142.8, 129.8, 129.0, 128.8, 125.6, 118.1, 36.0, 33.1, 26.3, 26.2; MS (ES^+ , Ar) m/z (rel intensity) 228 ($[\text{M}+2]^+$, 15), 227 (MH^+ , 100); HRMS

(ES⁺, Ar) calcd for C₁₅H₁₉N₂ (MH⁺) 227.1543, found 227.1542. No experimental data are available.³⁵

4-Butyl-2-phenyl-1H-imidazole (9p). Colorless liquid; Yield 75%, 30 mg; IR (neat, cm⁻¹) 3088 (br w), 2900 (w), 1499 (m), 1485 (s), 1460 (m), 1234 (vs), 1127 (m), 1034 (s), 936 (m), 694 (m); ¹H NMR (500 MHz, CDCl₃) δ 8.24 (br s, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 6.82 (s, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.59 (quint, *J* = 7.6 Hz, 2H), 1.33 (sextet, *J* = 7.6 Hz, 2H), 0.87 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 146.1, 137.9, 130.3, 129.0, 128.5, 125.4, 119.7, 31.6, 26.4, 22.5, 14.0; MS (ES⁺, Ar) *m/z* (rel intensity) 202 ([M+2]⁺, 11), 201 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₃H₁₇N₂ (MH⁺) 201.1386, found 201.1385.

4-(4-Methoxyphenyl)-2-(*p*-tolyl)-1H-imidazole (10b). Colorless solid; Yield 87%, 46 mg; mp 116–118 °C; IR (KBr, cm⁻¹) 3401 (m), 2928 (s), 2854 (m), 1505 (m), 1441 (m), 1247 (s), 1175 (m), 1143 (m), 1088 (m), 1027 (s), 834 (m), 739 (m); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.30 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.7 Hz, 2H), 7.52 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 3.75 (s, 3H), 2.32 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 158.0, 145.9, 137.4, 129.3, 128.0, 125.7, 124.9, 114.0, 55.1, 20.9; MS (ES⁺, Ar) *m/z* (rel intensity) 287 (MNa⁺, 49), 265 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₇H₁₇N₂O (MH⁺) 265.1335, found 265.1333.

2-(4-Chlorophenyl)-4-(4-methoxyphenyl)-1H-imidazole

(10c).^{15b} Pale yellow solid; Yield 79%, 45 mg; mp 149–151 °C (lit^{15b} 233–235 °C); IR (KBr, cm⁻¹) 2897 (br s), 1433 (s), 1245 (vs), 1142 (br s), 1026 (s), 835 (m), 738 (s); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.07 (d, *J* = 8.5 Hz, 2H), 8.02 (s, 1H), 7.82 (d, *J* = 8.7 Hz, 2H), 7.53 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H); ¹³C NMR (125 MHz, acetone-*d*₆) δ 158.8, 145.1, 133.2, 129.9, 128.8, 126.6, 125.9, 113.9, 54.6; MS (ES⁺, Ar) *m/z* (rel intensity) 307 (MNa⁺, 22), 287 ([M+2]⁺, 29), 285 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₆H₁₄ClN₂O (MH⁺) 285.0789, found 285.0788. The experimental data are consistent with those reported in the literature.^{15b}

2-(3-Chlorophenyl)-4-(4-methoxyphenyl)-1H-imidazole (10d).

Greenish liquid; Yield 83%, 47 mg; IR (neat, cm⁻¹) 3374 (br s), 2834 (m), 1616 (m), 1508 (s), 1393 (vw), 1248 (vs), 1179 (m), 1031 (m), 834 (m); ¹H NMR (500 MHz, CDCl₃) δ 9.27 (br s, 1H), 7.76 (s, 1H), 7.67–7.65 (m, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.26 (s, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.9 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 3.80 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 159.1, 145.9, 139.1, 134.8, 131.7, 130.1, 128.6, 126.6, 125.8, 124.9, 123.8, 117.7, 114.3, 55.5; MS (ES⁺, Ar) *m/z* (rel intensity) 286 ([M+2]⁺, 34), 285 (MH⁺, 100), 129 (41); HRMS (ES⁺, Ar) calcd for C₁₆H₁₄ClN₂O (MH⁺) 285.0789, found 285.0798.

4-(4-Methoxyphenyl)-2-(methylthio)-1H-imidazole (10e).

Yellow oily liquid; Yield 55%, 24 mg; IR (neat, cm⁻¹) 3160 (br m), 2955 (br w), 2839 (br m), 1652 (w), 1602 (m), 1507 (m), 1464 (w), 1302 (w), 1250 (vs), 1181 (m), 1030 (m), 834 (m); ¹H NMR (500 MHz, CDCl₃) δ 8.23 (br s, 1H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.21 (s, 1H), 6.87 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 2.53 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 159.0, 141.9, 139.3, 126.3, 125.2, 117.4, 114.3, 55.4, 17.5; MS (ES⁺, Ar) *m/z* (rel intensity) 237 ([MH+H₂O]⁺, 15), 221 (MH⁺, 100); HRMS (ES⁺, Ar) calcd for C₁₁H₁₃N₂OS (MH⁺) 221.0743, found 221.0743.

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