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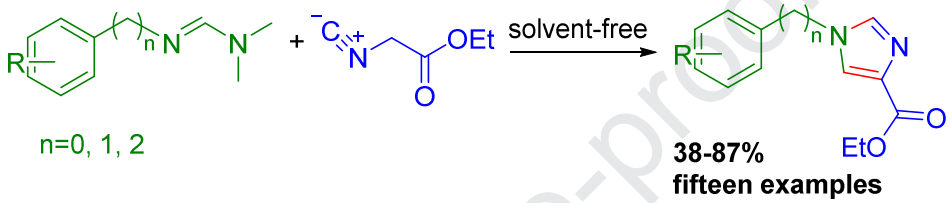

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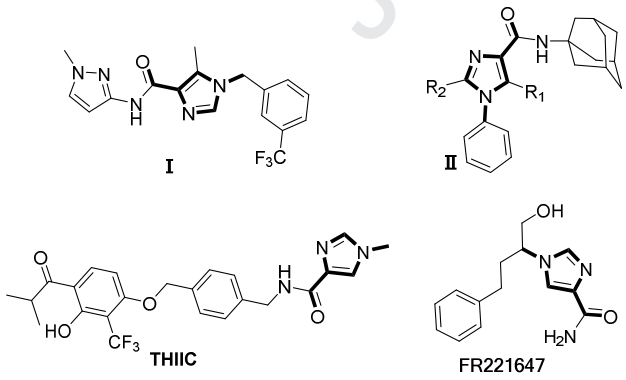
ABSTRACT

A simple and efficient protocol for cyclization between formamidines and ethyl isocyanoacetate has been described in the absence of metal catalyst and solvent. A series of 1-substituted-4-imidazolecarboxylates were synthesized in moderate to good yields with DABCO as base additive.

1. Introduction

Figure 1. Examples of biologically active 4-imidazolecarboxylates



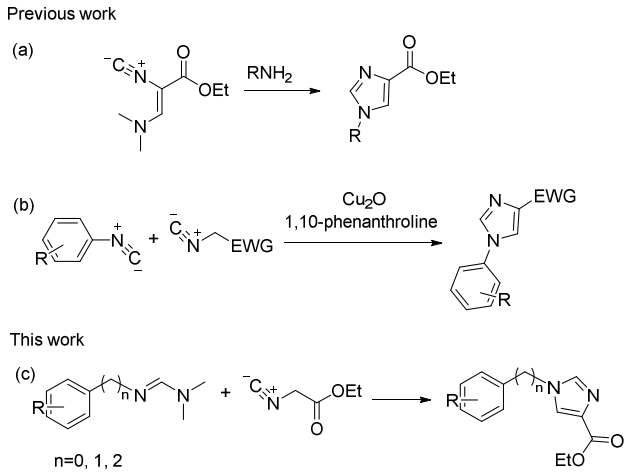
Formamidines are the important intermediates for the synthesis of heterocycles.[1] As a result, three categories of methods have been developed to prepare variously formamidines.[2] Interestingly，Besson and co-workers have reported a method for the rapid preparation of N-(2-cyano-4-nitrophenyl)-N, N-dimethylimidoformamide by microwave irradiation, yet only 5-nitroanthranilonitrile and anthranilonitrile have been reported as amine source.[3] Solvent-free reaction strategies have evolved as a green and sustainable approach in recent decades. Formamidines in organic synthesis have been proved to perform well in solvent-free conditions.[4]

4-imidazolecarboxylate, as the precursor of 4-imidazolecarboxamide, is a structural motif in numerous biologically active pharmacophores, as reported in the literature studies.[5] A particular example is 1-substituted-4-imidazolecarboxylates which get coupled with various amines to 1-substituted-4-imidazolecarboxamide, such as ADA Inhibitor (FR221647)[6], SCD-1 inhibitors (I)[7], CB2 receptor antagonists (II)[8], mGlu2 receptors (THIIC)[9], etc.

Although several synthetic routes using isocyanoacetates have been known[10-13], however, two representative approaches have been highlighted for the synthesis of the imidazole rings. Hela et al. described 1-alkyl-4-imidazolecarboxylates resulting from the reaction of anilines with ethyl 3-N, N-(dimethylamino)-2-isocyanoacrylate obtained by ethyl isocyanoacetate reacting with Bredereck's reagent.[11] However, the preparation of ethyl 3-N, N-(dimethylamino)-2-isocyanoacrylate is complex, and the yield is not excellent. Especially, on using aniline to prepare ethyl 1-phenyl-4-imidazolecarboxylate, a long reaction time is required, and the yield is modest (Scheme 1a). Yamamoto and co-workers have described an efficient synthetic procedure via cross-cycloaddition using copper (I) oxide as catalyst and 1,10-phenanthroline as ligand between two different isocyanides (Scheme 1b).[12] Roy et al. developed this approach a step further.[13] Moreover, isocyanides

resulted from dehydration of formamides, and proline was used as ligand to decrease the reaction temperature without reduced yields. However, the solvent-free reaction between formamidines and isocyanides has not yet been reported.

Scheme 1. The synthesis of 1-substituted-4-imidazolecarboxylates

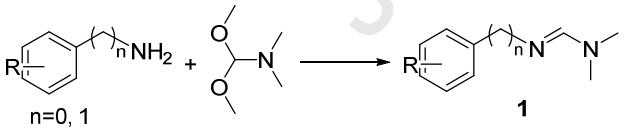


In this communication, we report the first ever synthesis of 1-substituted-4-imidazolecarboxylates using ethyl isocyanoacetate and corresponding formamidines, which, in turn, are prepared by the microwave synthesis of a variety of substituted aromatic and benzylic amines or phenethylamine with DMF-dimethylacetal (Scheme 1c).

2.Results and discussion

As part of our ongoing efforts towards the application of formamidines for the synthesis of 1-substituted-4-imidazolecarboxylates, we carried out the reaction of amines with DMF-DMA in solvent-free conditions by microwave irradiation. After optimization of the reaction conditions by varying the reaction time and temperature, we were able to obtain formamidines 1 at 80 □ and 150W in 10-25 minutes, with 85-99% yield (Table 1).

Table 1. Microwave-assisted synthesis of formamidines **1**[a]

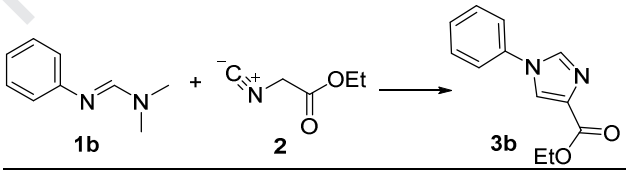


Entry	R, n	1	yield (%)[b]
1	**2-Br, n=0**	1a	85
2	**H,n=0**	1b	94
3	**4-NO_2,n=0**	1c	96
4	**4-F, n=0**	1d	99
5	**4-Cl, n=0**	1e	97
6	**4-I, n=0**	1f	96
7	**4-CH_3, n=0**	1g	99
8	**4-OCH_3, n=0**	1h	96
9	**2-OCH_3, n=0**	1i	91
10	**3-OCH_3, n=0**	1j	95
11	**H, n=1**	1k	94
12	**4-Cl, n=1**	1l	87
13	**4-CH_3, n=1**	1m	85
14	**4-CN, n=1**	1n	91
15	**H, n=2**	1o	92

[a] The mixture of amine (1.0 mmol), DMF-DMA (1.1 mmol) was stirred at 80□ using 10-25min of irradiation(150 W). [b] Isolated yield.

N, N-dimethyl-N'-phenylformimidamide (**1b**) and ethyl isocyanoacetate were chosen as the model reaction to find the optimal reaction conditions. Twelve reactions were run and the results are summarized in Table 2.

Table 2. Optimization of the reaction conditions



Entry	Base (equiv.)	Solvent	3	Yield (%) [a,b,c,d]
1	-	-	3b	23[a,c]
2	-	ethanol	3b	N.R[b,c]
3	-	butyl alcohol	3b	trace[b,c]
4	-	DMF	3b	N.R[b,c]
5	Et_3N (1.0)	-	3b	69[a,c]
6	DBU (1.0)	-	3b	12[b,c]
7	TEMED (1.0)	-	3b	59[a,c]
8	DMAP (1.0)	-	3b	10[b,c]
9	DABCO (1.0)	-	3b	87[a,c]
10	DABCO (1.0)	-	3b	59[a,d]
11	DABCO (0.5)		3b	51[a,c]
12	DABCO (1.5)		3b	87[a,c]

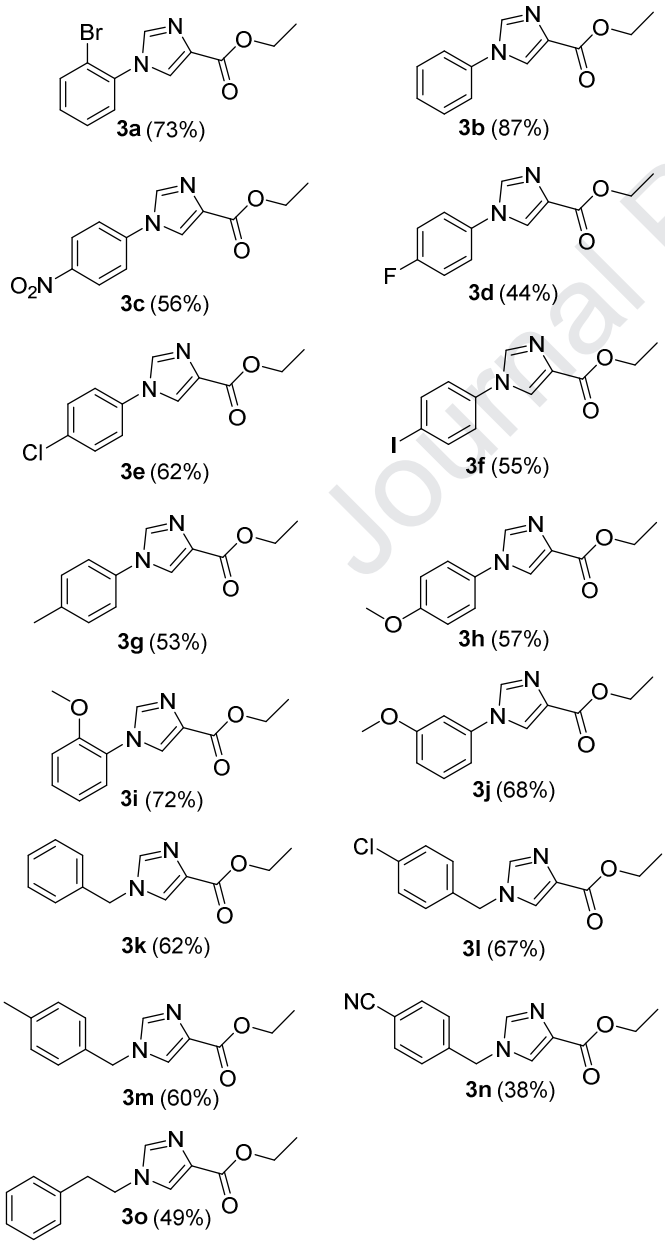
[a] Isolated yield. [b]Based on HPLC analysis. [c] Oil bath heating process. [d] Microwave heating process.

The product **3b** was obtained in 23% yield without base and solvent at 110□ for 24 h (Table 2, entry 1). No or trace desired product **3b** was observed with ethanol or N, N-dimethylformamide (DMF) or butyl alcohol as solvent at reflux temperature for 24 h (entry 2, 4, 3). These results led

to the choice of the solvent-free strategy due to the environmental benefits of solvent-free reactions. Et_3N (1.0 equiv.) has been examined as base which significantly improved the yield of **3b** (Table 2, entries 5). Different bases, such as DBU, TEMED, DMAP and DABCO (Table 2, entries 6−9) were screened, and the results show that DABCO was the best choice with the yield of **3b** reaching 87%. It was found that decreasing the amount of DABCO to 0.5 equiv. could reduce the yield of 3b to 51% (entry 11); while increasing the amount of DABCO to 1.5 equiv. did not further improve the yield of 3b (entry 12). (The structure has been confirmed by X-ray crystallographic analysis; see the Supporting Information (ESI).)

In order to improve the reaction efficiency, we compared the conventional heating process with the microwave heating process. The microwave heating failed to reduce the reaction time, the yield declined to 59% (Table 2, entry 10). With the established optimal conditions, we explored the substrate scope by testing various formamidines (**1a-o**) for the synthesis of 1-substituted-4-imidazolecarboxylates (Table 3).

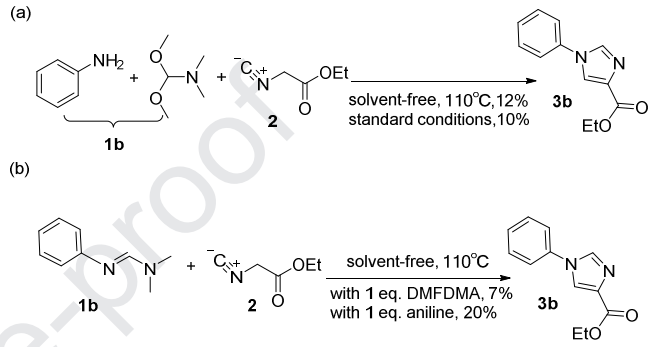
Table 3. Scope of 1-substituted-4-imidazolecarboxylates[a,b]



[a] Reaction condition: formamidines (1.0 mmol), ethyl isocyanoacetate (0.113 g, 1.0 mmol) under oil bath at 110□ with DABCO (0.112 g, 1.0 mmol) for 14h-24h. [b] Isolated yields.

To improve the utility of this protocol, a one-pot process was performed using aniline as the starting material; it was found that the reactions provided 3b in 10-12% yield, which were not good whether adding DABCO or not (Scheme 2a). In addition, the two-component reaction by adding DMF-DMA (1.0 eq.) or aniline (1.0 eq.) or additive free was used as a control experiment under the same conditions, producing **3b** in 7-23% yield (Scheme 2b; table 2, entry 1). The results suggest that DMF-DMA has an inhibitory effect on the reaction, and the two-component reaction of formamidine and ethyl isocyanoacetate is noted to be better.

Scheme 2. One-pot experiments [a, b]



[a]Standard conditions: **1b** (1.0 mmol), **2** (1.0 mmol), DABCO (1.0 mmol), solvent-free, 110□. [b]Isolated yield.

Conclusions

In conclusion, we have developed a new strategy for synthesizing 1-substituted-4-imidazolecarboxylates from formamidines and ethyl isocyanoacetate under solvent-free conditions. The process consists of two steps, the step one contains the rapid microwave-assisted preparation of formamidines and the step two results in cyclization to 1-substituted-4-imidazolecarboxylates in the absence of any metal catalyst. The new methodology is applied for the first time towards the preparation of 1-substituted-4-imidazolecarboxylates using formamidines, thus, confirming formamidines as useful building blocks for organic synthesis.

3.Experimental

General Information

All reagents and solvents were obtained from commercial suppliers and used without further purification. All reagents were weighed and handled in air at room temperature. Experimental microwave irradiation was carried out in a microwave single-mode reactor (Biotage, Initiator+). Melting points were recorded on a INESA (SGWX-4B) microscopic melting apparatus and uncorrected. ^{1}H NMR spectra were recorded on 400 MHz and ^{13}C NMR spectra were recorded on 125 MHz by using a Bruker Avance 400 spectrometer. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (TMS). HRMS data were recorded on Agilent 6530 Accurate-Mass Q-TOF LCMS spectrometer by ESI in positive mode. The X-ray single-crystal diffraction was performed on an Agilent Supernova CCD diffractometer instrument.

General procedure for the preparation of formamidines ***1a-o*****:**

Amine (10.0mmol) and DMF-dimethylaceta (11.0mmol) was transferred into the microwave vessels, these vessels were capped inside the synthesizer and transferred to the autosampler of the Biotage Initiator Sixty and heated to 80℃ at 150W for 10-25 minutes. These products were dried by vacuum and identified by NMR and HRMS, being in good agreement with the assigned structures.

Data for the formamidines ***1a-o*** *products:*

N'-(2-bromophenyl)-N,N-dimethylformimidamide (1a)

Light brown oil; yield: 85%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.52 (dd, J = 7.8, 1.5 Hz, 1H), 7.42 (s, 1H), 7.17 (td, J = 7.6, 1.5 Hz, 1H), 6.89 – 6.80 (m, 2H), 3.04 (d, J = 15.4 Hz, 6H).; ^{13}C NMR (101 MHz, Chloroform-d) δ 153.46, 150.08, 132.82, 128.17, 123.57, 121.06, 118.78, 40.29, 34.60; ESI-MS (m/z): Calcd for $C_9H_{12}BrN_2$ [(M + H)$^+$] 227.0184, Found 227.0195.

N,N-dimethyl-N'-phenylformimidamide (1b)

Light brown oil; yield: 94%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.40 (s, 1H), 7.20 – 7.12 (m, 2H), 6.91 (td, J = 7.3, 1.2 Hz, 1H), 6.87 (dd, J = 8.4, 1.3 Hz, 2H), 2.89 (s, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 153.48, 152.15, 129.02, 122.44, 121.24, 40.03, 34.67; ESI-MS (m/z): Calcd for $C_9H_{13}N_2$ [(M + H)$^+$] 149.1079, Found 149.1086.

N,N-dimethyl-N'-(4-nitrophenyl)formimidamide (1c)

Yellow solid; yield: 96%; mp 73-74 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.12 (dd, J = 9.1, 2.4 Hz, 2H), 7.60 (s, 1H), 6.98 (dd, J = 9.0, 1.9 Hz, 2H), 3.08 (d, J = 8.7 Hz, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 158.43, 153.93, 142.68, 125.26, 121.06, 40.59, 34.72; ESI-MS (m/z): Calcd for $C_9H_{12}N_3O_2$ [(M + H)$^+$] 194.0930, Found 194.0940.

N'-(4-fluorophenyl)-N,N-dimethylformimidamide (1d)

Pale brown solid; yield: 99%; mp 68-69 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.45 (s, 1H), 7.09 – 6.71 (m, 4H), 2.99 (d, J = 2.2 Hz, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 160.25, 157.87, 153.49, 148.33, 121.99 (d, J = 8.0 Hz), 115.43 (d, J = 21.9 Hz), 40.16, 34.46; ESI-MS (m/z): Calcd for $C_9H_{12}FN_2$ [(M + H)$^+$] 167.0985, Found 167.0987.

N'-(4-chlorophenyl)-N,N-dimethylformimidamide (1e)

Pale yellow oil; yield: 97%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.41 (s, 1H), 7.15 (dt, J = 6.5, 2.3 Hz, 2H), 6.87 – 6.78 (m, 2H), 2.94 (s, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 153.48, 150.79, 128.89, 127.29, 122.37, 40.19, 34.46; ESI-MS (m/z): Calcd for $C_9H_{12}ClN_2$ [(M + H)$^+$] 183.0689, Found 183.0697.

N'-(4-iodophenyl)-N,N-dimethylformimidamide (1f)

Pale brown oil; yield: 96%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.56 – 7.46 (m, 2H), 7.48 – 7.41 (m, 1H), 6.72 – 6.68 (m, 2H), 3.72 – 2.20 (m, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 153.47, 151.88, 137.84, 123.48, 85.45, 40.32, 34.55; ESI-MS (m/z): Calcd for $C_9H_{12}IN_2$ [(M + H)$^+$] 275.0045, Found 275.0053.

N,N-dimethyl-N'-(p-tolyl)formimidamide (1g)

Yellow oil; yield: 99%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.49 (s, 1H), 7.07 (d, J = 8.2 Hz, 2H), 6.96 – 6.69 (m, 2H), 3.00 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 153.36, 149.62, 131.73, 129.62, 120.98, 40.15, 34.54, 20.79; ESI-MS (m/z): Calcd for $C_{10}H_{15}N_2$ [(M + H)$^+$] 163.1235, Found 163.1236.

N'-(4-methoxyphenyl)-N,N-dimethylformimidamide (1h)

Light brown oil; yield: 96%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.43 (s, 1H), 6.86 (dd, J = 8.8, 2.2 Hz, 2H), 6.81 – 6.75 (m, 2H), 3.72 (s, 3H), 2.93 (s, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 155.43, 153.14, 145.60, 121.74, 114.29, 55.46, 40.01, 34.53; ESI-MS (m/z): Calcd for $C_{10}H_{15}N_2O$ [(M + H)$^+$] 179.1184, Found 179.1195.

N'-(2-methoxyphenyl)-N,N-dimethylformimidamide (1i)

Brown oil; yield: 91%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.48 (s, 1H), 6.96 (ddd, J = 9.6, 4.8, 1.9 Hz, 1H), 6.84 (td, J = 7.5, 1.5 Hz, 2H), 6.78 (dd, J = 7.5, 1.9 Hz, 1H), 3.81 (s, 3H), 2.99 (s, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 153.80, 152.45, 141.66, 123.06, 121.14, 120.97, 110.93, 55.71, 40.20, 34.51; ESI-MS (m/z): Calcd for $C_{10}H_{15}N_2O$ [(M + H)$^+$] 179.1184, Found 179.1194.

N'-(3-methoxyphenyl)-N,N-dimethylformimidamide (1j)

Brown oil; yield: 95%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.52 (d, J = 1.9 Hz, 1H), 7.18 – 7.10 (m, 1H), 6.61 – 6.50 (m, 3H), 3.81 – 3.75 (m, 3H), 3.00 (d, J = 2.5 Hz, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 160.38, 153.61, 153.53, 129.63, 113.37, 108.47, 106.89, 55.19, 40.22, 34.51; ESI-MS (m/z): Calcd for $C_{10}H_{15}N_2O$ [(M + H)$^+$] 179.1184, Found 179.1194.

N'-benzyl-N,N-dimethylformimidamide (1k)

Pale yellow oil; yield: 94%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.30 (s, 1H), 7.24 – 7.17 (m, 4H), 7.11 (ddd, J = 8.6, 5.6, 2.5 Hz, 1H), 4.37 (s, 2H), 2.79 (s, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 155.91, 142.35, 128.24, 127.43, 126.34, 59.56, 37.22; ESI-MS (m/z): Calcd for $C_{10}H_{15}N_2$ [(M + H)$^+$] 163.1235, Found 163.1244.

N'-(4-chlorobenzyl)-N,N-dimethylformimidamide (1l)

Pale yellow solid; yield: 87%; mp 96-97 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 (s, 1H), 7.26 – 7.17 (m, 4H), 4.39 (s, 2H), 2.86 (d, J = 3.7 Hz, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 155.99, 140.93, 131.89, 128.72, 128.27, 58.83, 37.24; ESI-MS (m/z): Calcd for $C_{10}H_{14}ClN_2$ [(M + H)$^+$] 197.0846, Found 197.0852.

N,N-dimethyl-N'-(4-methylbenzyl)formimidamide (1m)

White solid; yield: 85%; mp 79-80 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.38 (s, 1H), 7.19 (d, J = 7.8 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 4.43 (s, 2H), 2.87 (s, 6H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 155.76, 139.36, 135.78, 128.96, 127.43, 59.35, 37.20, 21.13; ESI-MS (m/z): Calcd for $C_{11}H_{17}N_2$ [(M + H)$^+$] 177.1392, Found 177.1390.

N'-(4-cyanobenzyl)-N,N-dimethylformimidamide (1n)

Pale brown oil; yield: 91%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.59 – 7.52 (m, 2H), 7.37 (d, J = 7.7 Hz, 3H), 4.47 (s, 2H), 2.88 (d, J = 1.9 Hz, 6H); ^{13}C NMR (101 MHz, Chloroform-d) δ 156.33, 148.25, 132.03, 127.93, 119.32, 109.90, 59.08, 41.68, 35.54; ESI-MS (m/z): Calcd for $C_{11}H_{14}N_3$ [(M + H)$^+$] 188.1188, Found 188.1193.

N,N-dimethyl-N'-phenethylformimidamide (1o)

Pale yellow oil; yield: 92%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.28 – 7.24 (m, 2H), 7.22 – 7.16 (m, 3H),

7.15 (s, 1H), 3.51 – 3.42 (m, 2H), 2.83 – 2.76 (m, 8H); ^{13}C NMR (101 MHz, Chloroform-d) δ 155.34, 140.75, 129.07, 128.19, 125.82, 58.21, 39.66, 37.14; ESI-MS (m/z): Calcd for $C_{11}H_{17}N_2$ [(M + H)$^+$] 177.1392, Found 177.1393.

General procedure for the preparation of formamidines ***3b***

To a mixture of N,N-dimethyl-N'-phenylformimidamide 1b (0.148g, 1 mmol), ethyl isocyanoacetate (0.113g, 1 mmol) and DABCO (0.112g, 1 mmol) at 110□ with stirring for 14h. The reaction mixture was passed through short column to give pure ethyl 1-phenyl-1H-imidazole-4-carboxylate (3b). ***Ethyl 1-phenyl-1H-imidazole-4-carboxylate (3b)*** Brown solid; yield: 87%; mp 82–83 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.96 (s, 2H), 7.60 – 7.50 (m, 2H), 7.49 – 7.37 (m, 3H), 4.41 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 161.00, 135.33, 133.02, 129.22, 127.77, 120.78, 60.07, 13.37; ESI-MS (m/z): Calcd for $C_{12}H_{12}N_2O_2Na$ [(M + Na)$^+$] 239.0796, Found 239.0800.

Ethyl 1-(2-bromophenyl)-1H-imidazole-4-carboxylate (3a)

Pale yellow oil; yield: 73%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.76 (d, J = 1.4 Hz, 1H), 7.71 (dd, J = 7.9, 1.2 Hz, 1H), 7.64 (d, J = 1.4 Hz, 1H), 7.43 (td, J = 7.6, 1.5 Hz, 1H), 7.37 – 7.29 (m, 2H), 4.36 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 162.70, 138.28, 135.74, 134.28, 134.11, 130.91, 128.71, 127.97, 126.33, 119.77, 60.75, 14.41; ESI-MS (m/z): Calcd for $C_{12}H_{11}BrN_2O_2Na$ [(M + Na)$^+$] 316.9902, Found 316.9903.

Ethyl 1-(4-nitrophenyl)-1H-imidazole-4-carboxylate (3c)

Grey solid; yield: 56%; mp 189–190 °C; ^{1}H NMR (400 MHz, DMSO-d6) δ 8.64 (d, J = 22.8 Hz, 2H), 8.37 (d, J = 8.6 Hz, 2H), 8.10 (d, J = 8.7 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d6) δ 162.38, 146.43, 141.33, 137.72, 134.94, 125.86, 124.54, 121.73, 60.46, 14.77; ESI-MS (m/z): Calcd for $C_{12}H_{11}N_3O_4Na$ [(M + Na)$^+$] 284.0647, Found 284.0662.

Ethyl 1-(4-fluorophenyl)-1H-imidazole-4-carboxylate (3d)

White solid; yield: 44%; mp 109-110 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.89 (d, J = 1.5 Hz, 1H), 7.79 (d, J = 1.4 Hz, 1H), 7.47 – 7.34 (m, 2H), 7.25 – 7.15 (m, 2H), 4.39 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 163.45, 162.69, 160.98, 136.48, 135.25, 132.74 (d, J = 3.3 Hz), 124.29, 123.85 (d, J = 8.7 Hz), 117.12 (d, J = 23.2 Hz), 60.83, 14.43; ESI-MS (m/z): Calcd for $C_{12}H_{11}FN_2O_2Na$ [(M + Na)$^+$] 257.0702, Found 257.0705.

Ethyl 1-(4-chlorophenyl)-1H-imidazole-4-carboxylate (3e)

Grey solid; yield: 62%; mp 128-130 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.94 (dd, J = 15.2, 1.4 Hz, 2H), 7.53 – 7.45 (m, 2H), 7.42 – 7.33 (m, 2H), 4.41 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 160.83, 135.36, 133.71, 133.67, 133.27, 129.40, 122.82, 122.09, 60.15, 13.36; ESI-MS (m/z): Calcd for $C_{12}H_{11}ClN_2O_2Na$ [(M + Na)$^+$] 273.0407, Found 273.0417.

Ethyl 1-(4-iodophenyl)-1H-imidazole-4-carboxylate (3f)

White solid; yield: 55%; mp 113-114 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.91 (q, J = 1.4 Hz, 1H), 7.83 (dq, J = 4.7, 2.7 Hz, 3H), 7.21 – 7.14 (m, 2H), 4.61 – 4.19 (m, 2H), 1.58 – 1.16 (m, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 162.59, 139.26, 136.06, 135.48, 123.67, 123.34, 93.18, 60.88, 14.44; ESI-MS (m/z): Calcd for $C_{12}H_{11}IN_2O_2Na$ [(M + Na)$^+$] 364.9763, Found 364.9771.

Ethyl 1-(p-tolyl)-1H-imidazole-4-carboxylate (3g)

White solid; yield: 53%; mp 60-61 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.92 (d, J = 1.4 Hz, 1H), 7.81 (d, J = 1.4 Hz, 1H), 7.29 (s, 4H), 4.40 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 162.86, 138.58, 136.36, 134.96, 134.12, 130.62, 124.15, 121.63, 60.75, 21.06, 14.46; ESI-MS (m/z): Calcd for $C_{13}H_{14}N_2O_2Na$ [(M + Na)$^+$] 253.0953, Found 253.0962.

Ethyl 1-(4-methoxyphenyl)-1H-imidazole-4-carboxylate (3h)

Pale yellow solid; yield: 57%; mp 65-66 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.91 (dd, J = 23.8, 1.3 Hz, 2H), 7.37 – 7.30 (m, 2H), 7.07 – 6.94 (m, 2H), 4.40 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 161.23, 158.74, 135.60, 132.88, 128.40, 123.46, 122.45, 114.16, 59.94, 54.67, 13.39; ESI-MS (m/z): Calcd for $C_{13}H_{14}N_2O_3Na$ [(M + Na)$^+$] 269.0902, Found 269.0916.

Ethyl 1-(2-methoxyphenyl)-1H-imidazole-4-carboxylate (3i)

Pale yellow solid; yield: 72%; mp 83-84 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.87 (d, J = 1.3 Hz, 1H), 7.75 (d, J = 1.4 Hz, 1H), 7.39 (ddd, J = 8.4, 7.5, 1.7 Hz, 1H), 7.28 (dd, J = 7.8, 1.7 Hz, 1H), 7.10 – 6.99 (m, 2H), 4.39 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 163.04, 152.56, 138.48, 133.76, 129.88, 126.42, 125.51, 121.12, 112.41, 60.60, 55.89, 14.47; ESI-MS (m/z): Calcd for $C_{13}H_{14}N_2O_3Na$ [(M + Na)$^+$] 269.0902, Found 269.0915.

Ethyl 1-(3-methoxyphenyl)-1H-imidazole-4-carboxylate (3j)

Brown solid; yield: 68%; mp 90-91 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.93 (d, J = 1.5 Hz, 1H), 7.83 (d, J = 1.5 Hz, 1H), 7.39 (t, J = 8.1 Hz, 1H), 6.97 (ddd, J = 7.9, 2.1, 0.9 Hz, 1H), 6.95 – 6.89 (m, 2H), 4.38 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 162.76, 160.81, 137.51, 136.30, 135.02, 130.98, 124.00, 113.74, 113.66, 107.82, 60.76, 55.64, 14.43; ESI-MS (m/z): Calcd for $C_{13}H_{14}N_2O_3Na$ [(M + Na)$^+$] 269.0902, Found 269.0917.

Ethyl 1-benzyl-1H-imidazole-4-carboxylate (3k)

Yellowish brown oil; yield: 62%; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.56 (dd, J = 12.5, 1.4 Hz, 2H), 7.39 – 7.32 (m, 3H), 7.16 (dd, J = 7.5, 2.0 Hz, 2H), 5.12 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 162.86, 138.08, 135.02, 134.46, 129.23, 128.75, 127.56, 125.33, 60.58, 51.36, 14.41; ESI-MS (m/z): Calcd for $C_{13}H_{14}N_2O_2$ Na[(M + Na)$^+$] 253.0953, Found 253.0961.

Ethyl 1-(4-chlorobenzyl)-1H-imidazole-4-carboxylate (3l)

Brown solid; yield: 67%; mp 74-75 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.57 – 7.52 (m, 2H), 7.37 – 7.31 (m, 2H), 7.13 – 7.07 (m, 2H), 5.11 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 161.71, 136.98, 133.78, 133.68, 132.46, 128.44, 127.83,

124.10, 59.63, 49.62, 13.38; ESI-MS (m/z): Calcd for $C_{13}H_{13}ClN_2O_2Na$ [$(M + Na)^+$] 287.0563, Found 287.0577.

Ethyl 1-(4-methylbenzyl)-1H-imidazole-4-carboxylate (3m)

Brown oil; yield: 60 %; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.54 (d, J = 13.1 Hz, 2H), 7.16 (d, J = 7.8 Hz, 2H), 7.06 (d, J = 7.8 Hz, 2H), 5.06 (s, 2H), 4.32 (q, J = 7.2 Hz, 2H), 2.33 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 161.84, 137.64, 136.98, 133.29, 130.93, 128.83, 126.60, 124.26, 59.51, 50.14, 20.11, 13.38; ESI-MS (m/z): Calcd for $C_{14}H_{16}N_2O_2Na$ [$(M + Na)^+$] 267.1109, Found 267.1101.

Ethyl 1-(4-cyanobenzyl)-1H-imidazole-4-carboxylate (3n)

Grey white solid; yield: 38%; mp 104-105 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.70 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 1.3 Hz, 2H), 7.28 (s, 2H), 5.24 (s, 2H), 4.38 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 161.56, 139.22, 137.10, 134.10, 132.03, 126.80, 124.08, 117.01, 111.85, 59.77, 49.64; ESI-MS (m/z): Calcd for $C_{14}H_{13}N_3O_2Na$ [$(M + Na)^+$] 278.0905, Found 278.0906.

Ethyl 1-phenethyl-1H-imidazole-4-carboxylate (3o)

Brown solid; yield: 49%; mp 51-52 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.52 (d, J = 1.4 Hz, 1H), 7.34 – 7.20 (m, 4H), 7.07 – 7.01 (m, 2H), 4.35 (q, J = 7.1 Hz, 2H), 4.20 (t, J = 7.0 Hz, 2H), 3.06 (t, J = 7.0 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 161.84, 136.87, 135.70, 133.03, 127.94, 127.54, 126.24, 123.92, 59.54, 48.05, 36.57, 13.38; ESI-MS (m/z): Calcd for $C_{14}H_{16}N_2O_2Na$ [$(M + Na)^+$] 267.1109, Found 267.1106.

Conflicts of interest

"There are no conflicts to declare".

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Highlights

A novel and green protocol for synthesis of 1-substituted-4-imidazolecarboxylates .

This cycloaddition reaction in the presence of DABCO under metal-free and solvent-free conditions.

Novel applications of formamidine for synthesis of heterocyclic compounds.

Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

None