One Pot $Pd(OAc)_2$-Catalysed 2,5-Diarylation of Imidazoles Derivatives

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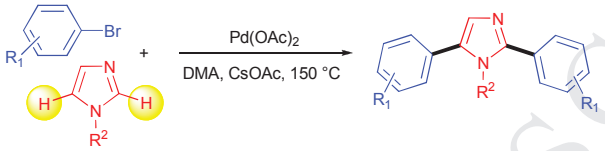

- No phosphine ligand on Pd
- No co-catalyst
- Good yields
- Oxidant free conditions
- Easily available substrates
- Wide functionnal group tolerance on ArBr

One Pot $Pd(OAc)_2$-Catalysed 2,5-Diarylation of Imidazoles Derivatives

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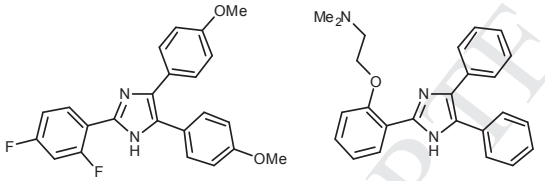
Abstract— The regioselective 2- or 5-arylation of imidazole derivatives with aryl halides using palladium catalysts has been described in recent years; whereas the arylation at both C2 and C5 carbons of imidazoles in high yields has not been performed. We found conditions allowing the access to these 2,5-diarylimidazoles via a one pot reaction. The choice of the base was found to be crucial to obtain these products in high yields. Using CsOAc as the base, DMA as the solvent and only 2 mol% of the phosphine-free $Pd(OAc)_2$ the catalyst, the target 2,5-diarylated imidazoles were obtained in moderate to good yields with a wide variety of aryl bromides. Substituents such as fluoro, trifluoromethyl, formyl, acetyl, propionyl, ester, nitro or nitrile on the aryl bromide were tolerated. Sterically congested aryl bromides or heteroaryl bromides can also be employed. Surprisingly the nature of the substituent at position 1 on the imidazole derivative exhibits a huge influence on the reaction.

1. Introduction

Aryl-substituted imidazoles including 2,5-diarylimidazoles are important structures due to their biological properties. For example, Fenflumizol and Trifenagrel are platelet aggregation inhibitors (Fig 1).



Fenflumizol Trifenagrel

Figure 1. Examples of bioactive 2,5-diarylimidazoles

Suzuki, Stille or Negishi palladium-catalysed cross-coupling reactions are among the most efficient methods to prepare 2,5-diarylimidazoles.[1] However, they require the previous preparation of an organometallic derivative. As early as 1990, Ohta et al. reported that the direct arylation of heteroaromatics with aryl halides via a C–H bond activation proceed in moderate to good yields using $Pd(PPh_3)_4$ as the catalyst.[2] Since these exciting results, the Pd-catalysed direct arylation of heteroaryls using aryl halides as coupling partners has proved to be a very powerful method for a simpler and greener access to a wide variety of arylated heterocycles, as the major by-products of the reaction are a base associated to HX, instead of metallic salts produced under more classical cross-coupling procedures.[3] Moreover, the method avoids the preliminary preparation of an organometallic derivative. However, so far, the direct arylation of imidazoles has attracted less attention than the arylation of thiophenes or thiazoles, and in most cases mono-arylations have been described.[4-6] The first example of direct 5-arylation of imidazoles using chloropyrazines as coupling partners and 5 mol% $Pd(PPh_3)_4$ as the catalyst was reported by Ohta and co-workers in 1992.[4] Since these results, several groups described conditions allowing the intermolecular Pd-catalysed direct 2- or 5-arylation of imidazoles.[5,6]

So far, to our knowledge, only a few examples of Pd-catalysed arylations at both C2 and C5 carbons of imidazoles in one pot have been described.[7-9] In 1998, Miura et al. reported the regioselectivity of the arylation of 1-methylimidazole using various reaction conditions.[8a] In the presence of bromobenzene, they observed the formation of a mixture of 5-arylation and 2,5-diarylation products in a 54:24 ratio (Scheme 1, top). They also reported that the addition of 2 equiv. of CuI to the reaction mixture, using iodobenzene as the coupling partner, drastically modify the selectivity of the reaction, as a mixture of C2 and C2,C5 arylation products in a 37:40 ratio was obtained. It should be noted that CuI itself promotes the C2 arylation of imidazole. Bellina, Rossi and co-workers also studied the influence of several parameters for the arylation of imidazoles, and succeeded in a few cases to obtain directly the 2,5-diarylated

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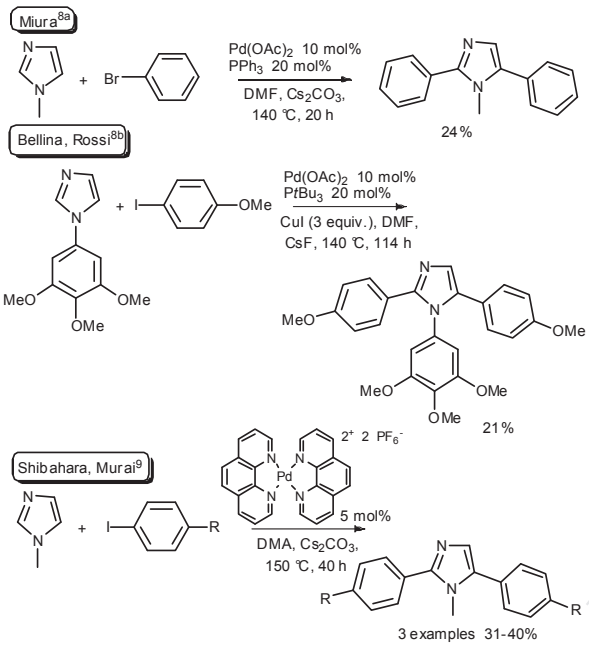
imidazoles although in moderate yields.[8b] A few 2,5-diarylimidazoles have also been prepared by Shibahara, Murai et al. using a 1,10-phenanthroline containing Pd catalyst and aryl iodides as coupling partners.[9] However, so far sequential Pd-catalysed direct arylations remains the most reliable method to prepare 2,5-diarylimidazoles in good yields.[10]



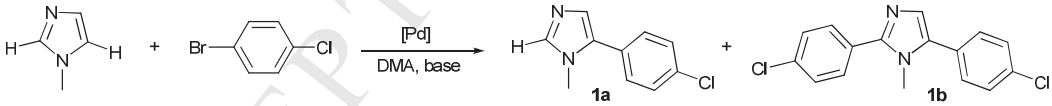
Scheme 1. Reported examples of Pd-catalysed one pot access to 2,5-diarylimidazoles

Therefore, the discovery of effective conditions, for the direct coupling of aryl halides at both C2 and C5 positions of imidazole derivatives in one pot, would constitute a considerable advantage allowing a simpler access to 2,5-diarylimidazoles.

Here, we wish to (i) report that $Pd(OAc)_2$ catalyst without any additional ligand promotes the direct access to 2,5-diarylimidazoles in one pot, (ii) report on the reaction scope using a large set of electronically and sterically diverse aryl bromides, (iii) reveal the influence of the imidazole *N*-substituent.

2. Results and discussion

We have recently reported the direct 5-arylation of a range of imidazole derivatives using a phosphine-free palladium catalyst.[11] Based on these results, for this study DMA was initially chosen as the solvent and KOAc as the base. The reactions were performed at 150 °C under argon in the presence of $Pd(OAc)_2$ catalyst. Using only 0.5 mol% $Pd(OAc)_2$, the reaction of 3 equiv. of 4-bromochlorobenzene with 1 equiv. of 1-methylimidazole affords the mono- and di-arylation products **1a**:**1b** in a 73:27 ratio and the target product **1b** was isolated in a low yield of 18% (Table 1, entry 1). Then, we examined the influence of the amount of catalyst and base for this reaction (Scheme 2, Table 1, entries 2-5). A larger excess (4 equiv.) of KOAc base affords the products **1a**:**1b** in a 68:32 ratio. In the presence of 1 or 2 mol-% $Pd(OAc)_2$ instead of 0.5 mol%, an almost equimolar mixture of **1a**:**1b** was obtained. A longer reaction time (48 h instead on 20 h) led to products **1a**:**1b** in 23:77 ratio and **1b** was isolated in 62% yield (Table 1, entry 5). An important effect of the acetate anion was observed. The use of CsOAc instead of KOAc in the presence of 2 mol% $Pd(OAc)_2$ gave **1a**:**1b** in 12:88 ratio and **1b** in 70% yield; whereas, NaOAc (2 equiv.) led to products **1a**:**1b** in 89:11 ratio and allowed to isolate **1a** in 64% yield (Table 1, entries 8 and 10). A lower reaction temperature (120 °C) affords products **1a**:**1b** in 92:8 ratio (Table 1, entry 9).



Scheme 2.

Table 1. Influence of the reaction conditions for palladium catalysed arylation of 1-methylimidazole with 4-bromochlorobenzene (Scheme 2)

Entry	Catalyst (mol%)	Base (equiv.)	Time (h)	Ratio **1a**:**1b**	Yield in **1b** (%)
1	0.5	KOAc (3)	20	73:27	18
2	0.5	KOAc (4)	20	68:32	
3	1	KOAc (4)	20	52:48	
4	2	KOAc (4)	20	52:48	
5	1	KOAc (4)	48	23:77	62
6	1	KOAc (3) Cs_2CO_3 (3)	20	44:56	
7	1	CsOAc (4)	48	15:85	
8	2	CsOAc (4)	48	**12:88**	70
9	2	CsOAc (4)	48	92:8[a]	
10	0.5	NaOAc (2)	20	**89:11**[b]	64

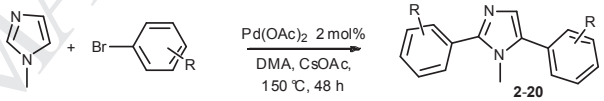
Conditions: $Pd(OAc)_2$ 0.5-2 mol%, 4-bromochlorobenzene (3 equiv.), 1-methylimidazole (1 equiv.), DMA, 150 °C, 20 h, isolated yields. [a] 120°C. [b] 4-Bromochlorobenzene (1.2 equiv.), 1-methylimidazole (1 equiv.), yield in **1a**.

Then, using the most effective reaction conditions (DMA, CsOAc, $Pd(OAc)_2$, 150 °C, 48 h) we explored the scope of this reaction using *para*-, *meta*- and *ortho*-substituted aryl bromides and also some heteroaryl bromides employing 1-methylimidazole as the coupling partner (Scheme 3, Table 2).

First, we investigated the reaction of 1-methylimidazole with several *para*-substituted aryl bromides (Scheme 3, Table 2). In most cases, the reaction proceeds very smoothly in the presence of 2 mol% $Pd(OAc)_2$ catalyst. With electron deficient aryl bromides such as 4-bromoacetophenone, 4-bromopropiophenone, ethyl 4-bromopropionate, 4-bromobenzaldehyde or 4-bromobenzonitrile, yields of 55-65% in **2-6** were obtained (Table 2, entries 1-5). We also obtained satisfactory results using 4-fluorobromobenzene, bromobenzene or even the electron-rich 4-bromotoluene and 4-bromoanisole to afford **8-11** in 78-81% yields (Table 1, entries 7 and 10). On the other hand, the use of 4-bromonitrobenzene affords the diarylated imidazole **7** in only 32% yield due to the formation of a large amount of mono-arylated 1-methylimidazole (Table 2, entry 6). The general pattern revealed by these results shows that the electron-withdrawing substituents are slightly less favourable to obtaining the desired 2,5-diarylimidazoles. The presence of an electron-deficient aryl group at C5 of imidazole appears to disfavour the second arylation at carbon C2.

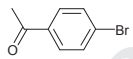
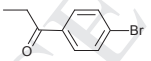
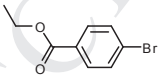
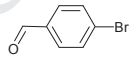
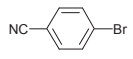
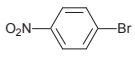
The influence of the presence of *meta*-substituents on the aryl bromide is also reported in the Table 2. As expected, relatively similar yields than in the presence of the *para*-substituted substrates were obtained for the reactions performed with 3-bromobenzonitrile, 3-(trifluoromethyl)bromobenzene or 3-bromotoluene using again 2 mol% $Pd(OAc)_2$ catalyst (Table 2, entries 12-14). 3-Bromonitrobenzene, affords **12** in higher yield than the reaction performed with 4-bromonitrobenzene (Table 2, entry 11). Surprisingly, with 3,5-bis(trifluoromethyl)bromobenzene, a mixture of di- and tri-arylation products **16a** and **16b** was obtained in a 57:43 ratio (Table 2, entry 15).

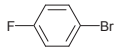
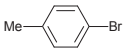
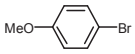
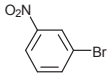
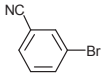
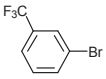
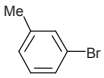
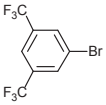
Then, we examined the reactivity of 1-methylimidazole with a set of *ortho*-substituted aryl bromides. *Ortho*-substituents on the aryl bromides generally have an important effect on the reaction rates of palladium-catalysed reactions due to their steric and/or coordination properties. The expected 2,5-diaryl-1-methylimidazoles **17-19** were obtained in moderate to good yields. In some cases, similar yields than in the presence of the *para*-substituted aryl bromides were obtained. For example, the coupling of 2-bromobenzonitrile or 2-fluorobromobenzene proceeds nicely to afford **17** and **18** in 78% and 59% yields, respectively (Table 4, entries 16 and 17). Heteroaryl bromide, 3-bromopyridine was also found to be a suitable reactant, as **20** was obtained in 72% yield (Table 2, entry 19).



Scheme 3.

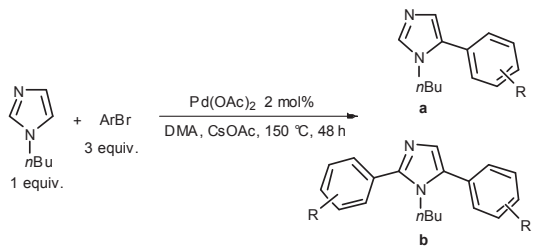
Table 2. Palladium catalysed diarylation of 1-methylimidazole with aryl bromides (Scheme 3)

Entry	Aryl bromide	Product	Yield (%)
1		**2**	59
2		**3**	65
3		**4**	55
4		**5**	62
5		 **6**	60
6		**7**	32

7		**8**	78
8		**9**	80
9		**10**	81
10		**11**	78
11		**12**	62
12		**13**	60
13		**14**	59
14		**15**	79
15		**16a**	48[a]
16		**17**	78
17		**18**	59
18		**19**	54
19		**20**	72

Conditions: $Pd(OAc)_2$ (0.02 equiv.), ArBr (3 equiv.), 1-methylimidazole (1 equiv.), CsOAc (4 equiv.), DMA, 150 °C, 48 h, isolated yields. [a] The formation of a large amount of tri-arylation product **16b** was observed (ratio **16a**:**16b** 57:43).

With 1-*n*-butylimidazole, using similar reaction conditions, low yields of the desired 2,5-diarylation products **21b-23b** were obtained (Scheme 4). Surprisingly, with this imidazole derivative the formation of very large amounts of mono-arylation products was observed. With 4-bromochlorobenzene or 4-bromotoluene, mono-arylation products **21a** and **23a** and di-arylation products **21b** and **23b** were formed in 71:29 and 69:31 ratios, respectively. These results reveal that, unexpectedly the presence of a *n*-butyl substituent instead of a methyl substituent at position 1 of an imidazole dramatically decreases its reactivity for the second arylation at C2.

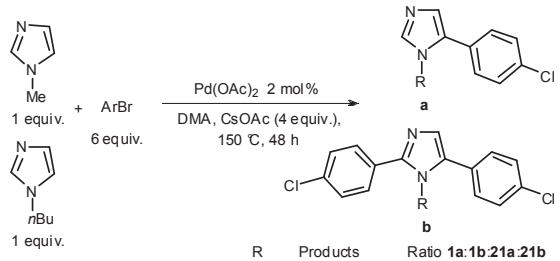


R	Ratio **a**:**b**	Product	Yield in **b** (%)
4-Cl	71:29	**21a:21b**	24
3,5-diCF_3	14:43:43*	**22a:22b:22c**	35
4-Me	69:31	**23a:23b**	25

*: 2,4,5-Triarylation product **22c** also obtained in 43% selectivity and 33% yield

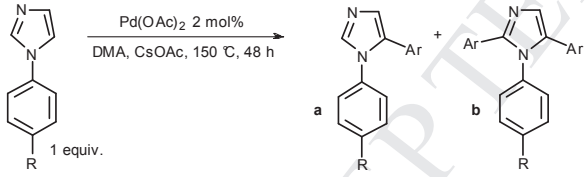
Scheme 4.

In order to gain more insight into the lower reactivity of 1-*n*-butylimidazole *vs* 1-methylimidazole, a competition reaction to probe the substituent preference of this catalyst system for such couplings was performed (Scheme 5). From an equimolar mixture of 1-methylimidazole and 1-*n*-butylimidazole using 6 equiv. of 4-bromochlorobenzene as the coupling partner, in the presence of 2 mol-% $Pd(OAc)_2$ catalyst, the formation of a mixture of **1a**:**1b**:**21a**:**21b** in a 27:27:43:3 ratio was observed. This result confirms that a *n*-butyl substituent at position 1 of imidazole is strongly deactivating for the second arylation.



Scheme 5.

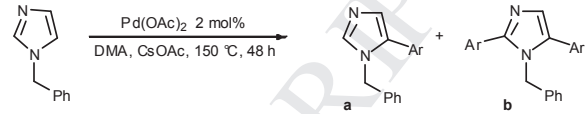
The influence of an aryl group at position 1 on imidazole was also investigated (Scheme 6). This copper and phosphine-free procedure was found to afford selectively in all cases the mono C5-arylated products **24a**-**27a**. The presence of a *para*-methoxy or a *para*-formyl substituent on the 1-arylimidazole has a minor influence on the selectivity and yield of the reaction. Again, the presence of trifluoromethyl substituents on bromobenzene favours the formation of 2,5-diarylated products **25b** and **27b** although in very low yields.



R	Ar	Ratio **a**:**b**	Product	Yield in **a** (%)
OMe	4-ClC_6H_4	100:0	**24a**:**24b**	62
OMe	3,5-di(CF_3)C_6H_3	87:13	**25a**:**25b**	75
CHO	4-ClC_6H_4	100:0	**26a**:**26b**	53
CHO	3,5-di(CF_3)C_6H_3	95:5	**27a**:**27b**	52

Scheme 6.

We then turned our attention to the reactivity of 1-benzylimidazole for the Pd-catalysed 2,5-diarylations, as the deprotection of imidazoles bearing benzyl substituents is easier than the corresponding 1-methylimidazoles (Scheme 7). We selected our previous best reaction conditions, i.e, 2 mol% $Pd(OAc)_2$ catalyst in the presence of 4 equiv. of CsOAc as base in DMA at 150 ºC. In the presence of 4-bromobenzonitrile, only the formation of the mono-5-arylated imidazole **28a**, without cleavage of the benzyl group, was observed. On the other hand, the reaction with 3,5-bis(trifluoromethyl)bromobenzene affords a mixture of the mono- di- and tri-arylation products **29a**, **29b** and **29c** in a 15:40:45 ratio. From 4-chlorobromobenzene and 4-bromotoluene, mixtures of mono- and di-arylation products were obtained. These selectivities are very similar to those observed in the course of the coupling with 1-*n*-butylimidazole (Scheme 2). Therefore, for the access to *N*-benzyl substituted 2,5-diarylimizazoles, the sequential arylation procedure reported by Bellina, Rossi et al. using 5 mol% $Pd(OAc)_2$ associated to 2 equiv. of CuI for the second arylation at C2 should be preferred.[10a]



Ar	Ratio **a**:**b**	Product	Yield in **a** (%)
4-CNC_6H_4	100:0	**28a**:**28b**	41
3,5-di(CF_3)C_6H_3	15:40:45	**29a**:**29b**:**29c***	32 of **29b**
4-ClC_6H_4	70:30	**30a**:**30b**	44
4-MeC_6H_4	50:50	**31a**:**31b**	31

*: 2,4,5-Triarylation product **29c** also obtained in 45% selectivity and in 34% yield

Scheme 7.

In conclusion, we report here for the first time a simple one-pot catalytic method leading to the direct synthesis of 2,5-diarylimidazoles in good yields. We have established that, a phosphine-free and copper-free procedure using $Pd(OAc)_2$ catalyst, CsOAc as base in the presence of aryl bromides as coupling partners promotes the 2,5-diarylation of 1-methylimidazole. A wide range of functions such as fluoro, acetyl, formyl, propionyl, carboxylate, nitrile or nitro on the aryl bromide are tolerated. Some sterically hindered aryl bromides and heteroaromatic substrate 3-bromopyridines have also been employed successfully. The substituents at position 1 on imidazole were found to exhibit a very important influence on the products distribution. It should be noted that, despite their interest, most of the products prepared by this method are new, indicating a relatively limited access to such compounds using more traditional cross-coupling procedures. This procedure employs a commercially available, phosphine-free and air stable palladium source. Therefore, there is no need to eliminate phosphine derivatives at the end of the reaction. Moreover, a very wide variety of aryl bromides are commercially available. These are practical advantages of this reaction.

3. Experimental

General Remarks: All reactions were run under argon in Schlenk tubes using vacuum lines. DMA analytical grade was not distilled before use. CsOAc (99%) was used. Commercial aryl bromides and imidazoles were used without purification. The reactions were followed by GC and NMR. ^1H and ^{13}C spectra were recorded with a Bruker 400 MHz spectrometer in $CDCl_3$ solutions. Chemical shifts are reported in ppm relative to $CDCl_3$ (7.25 for ^1H NMR and 77.0 for ^{13}C NMR). Flash chromatography was performed on silica gel (230–400 mesh).

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Experimental section

General procedure

In a typical experiment, the aryl bromide (3 mmol), imidazole derivative (1 mmol), CsOAc (1.303 g, 4 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), were dissolved in DMA (5 mL) under an argon atmosphere. The reaction mixture was stirred at 150 °C for 48h. After evaporation of the solvent, the product was purified by silica gel column chromatography.

5-(4-Chlorophenyl)-1-methylimidazole (1a)[8c]

From 4-bromochlorobenzene (0.230 g, 1.2 mmol), 1-methylimidazole (0.082 g, 1 mmol) and NaOAc (0.164 g, 2 mmol) with $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), product **1a** was obtained in 64% (0.123 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.01 (s, 1H), 3.57 (s, 3H).

2,5-Bis(4-chlorophenyl)-1-methylimidazole (1b)

From 4-bromochlorobenzene (0.574 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **1b** was obtained in 70% (0.212 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.12 (s, 1H), 3.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 135.3, 134.6, 134.4, 130.1, 129.9, 129.2, 129.0, 128.5, 128.2, 127.1, 33.9. $C_{16}H_{12}Cl_2N_2$ (303.19): Calcd C 63.38, H 3.99, N 9.24; Found C 63.55, H 4.09, N 9.14.

1,1'-(4,4'-(1-methylimidazole-2,5-diyl)bis(4,1-phenylene))diethanone (2)[7b]

From 4-bromoacetophenone (0.597 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **2** was obtained in 59% (0.187 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 3.70 (s, 3H), 2.60 (s, 3H), 2.59 (s, 3H).

1,1'-(4,4'-(1-Methylimidazole-2,5-diyl)bis(4,1-phenylene))dipropan-1-one (3)

From 4-bromopropiophenone (0.639 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **3** was obtained in 65% (0.225 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.98 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.27 (s, 1H), 3.71 (s, 3H), 2.95 (q, J = 7.5 Hz, 4H), 1.15 (t, J = 7.5 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 200.0, 149.0, 136.9, 136.2, 135.3, 134.1, 133.9, 128.9, 128.6, 128.4, 128.3, 34.4, 32.0, 31.9, 8.3, 8.2. $C_{22}H_{22}N_2O_2$ (346.42): Calcd C 76.28, H 6.40, N 8.09; Found C 76.08, H 6.21, N 7.88.

Diethyl 4,4'-(1-methylimidazole-2,5-diyl)dibenzoate (4)

From ethyl 4-bromobenzoate (0.687 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **4** was obtained in 55% (0.208 g) yield. ^{1}H NMR (400 MHz, DMSOd_6) δ 8.10 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.39 (s, 1H), 4.36 (q, J = 7.5 Hz, 4H), 3.77 (s, 3H), 1.35 (t, J = 7.5 Hz, 6H). ^{13}C NMR (100 MHz, DMSOd_6) δ 165.9, 165.8, 149.0, 135.3, 135.2, 134.6, 130.1, 130.0, 129.8, 129.5, 129.2, 129.1, 128.5, 61.4, 61.3, 34.8, 14.6. $C_{22}H_{22}N_2O_4$ (378.42): Calcd C 69.83, H 5.86, N 7.40; Found C 69.71, H 5.70, N 7.55.

4,4'-(1-Methylimidazole-2,5-diyl)dibenzaldehyde (5)

From 4-bromobenzaldehyde (0.555 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **5** was obtained in 62% (0.180 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 10.01 (s, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.33 (s, 1H), 3.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 191.4, 149.3, 136.2, 135.9, 135.6, 131.5, 130.3, 130.0, 129.8, 129.2, 128.7, 127.5, 34.4. $C_{18}H_{14}N_2O_2$ (290.32): Calcd C 74.47, H 4.86, N 9.65; Found C 74.55, H 4.99, N 9.47.

4,4'-(1-Methylimidazole-2,5-diyl)dibenzonitrile (6)

From 4-bromobenzonitrile (0.546 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **6** was obtained in 60% (0.170 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 4H), 7.55 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 134.9, 134.1, 133.9, 132.8, 132.6, 129.5, 129.3, 128.8, 118.4, 118.3, 112.9, 112.0, 34.4. $C_{18}H_{12}N_4$ (284.31): Calcd C 76.04, H 4.25, N 19.71; Found C 76.18, H 4.08, N 19.99.

1-Methyl-2,5-bis(4-nitrophenyl)-imidazole (7)

From 4-bromonitrobenzene (0.606 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **7** was obtained in 32% (0.104 g) yield. ^{1}H NMR (400 MHz, DMSOd_6) δ 8.39 (d, J = 8.4 Hz, 2H), 8.36 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.4 Hz, 2H), 7.55 (s, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, DMSOd_6) δ 148.7, 147.6, 147.0, 136.8, 136.4, 135.1, 130.9, 130.0, 129.3, 124.6, 124.3, 35.0. $C_{16}H_{12}N_4O_4$ (324.29): Calcd C 59.26, H 3.73, N 17.28; Found C 59.04, H 3.49, N 17.38.

2,5-Bis(4-fluorophenyl)-1-methylimidazole (8)

From 4-bromofluorobenzene (0.525 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **8** was obtained in 78% (0.210 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.55 (m, 2H), 7.40-7.30 (m, 2H), 7.15-7.00 (m, 5H), 3.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ163.1 (d, J = 249.0 Hz), 162.7 (d, J = 249.0 Hz), 148.4, 134.4, 130.7 (d, J = 8.3 Hz), 130.5 (d, J = 8.3 Hz), 127.4, 126.9 (d, J = 3.3 Hz), 126.2 (d, J = 3.3 Hz), 115.9 (d, J = 17.3 Hz), 115.7 (d, J = 17.3 Hz), 33.6. $C_{16}H_{12}F_2N_2$ (270.28): Calcd C 71.10, H 4.48, N 10.36; Found C 71.02, H 4.34, N 10.17.

1-Methyl-2,5-diphenylimidazole (9)[9b]

From 4-bromobenzene (0.471 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **9** was obtained in 80% (0.187 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2H), 7.45-7.25 (m, 8H), 7.14 (s, 1H), 3.62 (s, 3H).

1-Methyl-2,5-di*p*-tolylimidazole (10)

From 4-bromotoluene (0.513 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **10** was obtained in 81% (0.212 g) yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 4H), 7.23-7.17 (m, 4H), 7.10 (s, 1H), 3.58 (s, 3H), 2.34 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 139.0, 138.0, 135.3, 129.5, 129.3, 128.8, 128.7, 127.4, 127.1, 126.2, 33.8, 21.4, 21.3. $C_{18}H_{18}N_2$ (262.35): Calcd C 82.41, H 6.92, N 10.68; Found C 82.50, H 6.98, N 10.89.

2,5-Bis(4-methoxyphenyl)-1-methylimidazole (11)[8c]

From 4-bromoanisole (0.561 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **11** was obtained in 78% (0.229 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.04 (s, 1H), 6.93 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.55 (s, 3H).

1-Methyl-2,5-bis(3-nitrophenyl)-imidazole (12)

From 3-bromonitrobenzene (0.606 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **12** was obtained in 62% (0.201 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.35-8.15 (m, 3H), 8.05 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.25 (s, 1H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 148.4, 147.9, 134.7, 134.3, 134.0, 131.9, 131.3, 130.1, 130.0, 129.4, 123.8, 123.4, 123.1, 123.0, 34.0. $C_{16}H_{12}N_4O_4$ (324.29): Calcd C 59.26, H 3.73, N 17.28; Found C 59.40, H 3.61, N 17.10.

3,3'-(1-Methylimidazole-2,5-diyl)dibenzonitrile (13)

From 3-bromobenzonitrile (0.546 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **13** was obtained in 60% (0.170 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.75-7.65 (m, 4H), 7.61 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.23 (s, 1H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 134.1, 133.4, 133.2, 133.1, 132.4, 132.3, 132.1, 130.2, 130.1, 130.0, 118.0, 117.9, 113.6, 113.3, 34.2. $C_{18}H_{12}N_4$ (284.31): Calcd C 76.04, H 4.25, N 19.71; Found C 76.29, H 4.22, N 19.50.

1-Methyl-2,5-bis(3-(trifluoromethyl)phenyl)-imidazole (14)

From 3-bromobenzotrifluoride (0.675 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **14** was obtained in 59% (0.218 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.65-7.50 (m, 6H), 7.21 (s, 1H), 3.63 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 134.5, 131.9, 131.8, 131.5 (q, J = 20.4 Hz), 131.4, 131.1 (q, J = 20.4 Hz), 130.7, 129.4, 129.2, 128.6, 125.7, (q, J = 3.7 Hz), 125.6 (q, J = 3.7 Hz), 125.3 (q, J = 3.7 Hz), 124.8 (q, J = 3.7 Hz), 122.5, 33.8. $C_{18}H_{12}F_6N_2$ (370.29): Calcd C 58.38, H 3.27, N 7.57; Found C 58.47, H 3.45, N 7.42.

1-Methyl-2,5-di*m*-tolylimidazole (15)

From 3-bromotoluene (0.513 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **15** was obtained in 79% (0.207 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.22-7.10 (m, 5H), 3.59 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 149.1, 138.5, 138.4, 135.5, 130.3, 130.0, 129.7, 129.5, 128.8, 128.7, 128.4, 126.7, 125.8,

125.7, 33.8, 21.5, 21.4. $C_{18}H_{18}N_2$ (262.35): Calcd C 82.41, H 6.92, N 10.68; Found C 82.27, H 6.90, N 10.51.

2,5-bis(3,5-bis(trifluoromethyl)phenyl)-1-methylimidazole (16a)

From 3,5-bis(trifluoromethyl)bromobenzene (0.879 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **16a** was obtained in 48% (0.243 g) yield. The 2,4,5-triarylated imidazole **16b** was also isolated in 30% (0.215 g) yield. **16a:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 2H), 7.89 (s, 1H), 7.85 (s, 3H), 7.31 (s, 1H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 133.8, 132.7 (q, J = 26.2 Hz), 132.1 (q, J = 26.2 Hz), 131.5, 129.6, 128.5, 128.4, 124.3, 122.8 (quint., J = 3.6 Hz), 122.1 (quint., J = 3.6 Hz), 121.6, 118.9, 33.9. $C_{20}H_{10}F_{12}N_2$ (506.29): Calcd C 47.45, H 1.99, N 5.53; Found C 47.40, H 2.09, N 5.36. **16b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 2H), 8.00 (s, 1H), 7.96 (s, 1H), 7.84 (s, 4H), 7.66 (s, 1H), 3.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 136.4, 134.0, 132.3 (q, J = 34.8 Hz), 131.5 (q, J = 34.8 Hz), 130.9 (q, J = 34.8 Hz), 130.7, 130.6, 129.6 (m), 128.6, 128.0 (m), 122.4 (m), 122.2 (m), 120.0 (m), 121.7 (q, J = 270.0 Hz), 121.6 (q, J = 270.0 Hz), 121.5 (q, J = 270.0 Hz), 32.6. $C_{28}H_{12}F_{18}N_2$ (718.38): Calcd C 46.81, H 1.68, N 3.90; Found C 46.99, H 1.88, N 3.99.

2,2'-(1-Methylimidazole-2,5-diyl)dibenzonitrile (17)

From 2-bromobenzonitrile (0.546 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **17** was obtained in 78% (0.221 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 2H), 7.70-7.65 (m, 3H), 7.58-7.45 (m, 3H), 7.38 (s, 1H), 3.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 134.1, 133.7, 133.6, 133.2, 133.0, 132.9, 131.7, 131.6, 131.3, 130.5, 129.7, 129.0, 117.9, 117.8, 113.1, 33.3. $C_{18}H_{12}N_4$ (284.31): Calcd C 76.04, H 4.25, N 19.71; Found C 76.09, H 4.31, N 19.57.

2,5-Bis(2-fluorophenyl)-1-methylimidazole (18)

From 2-bromofluorobenzene (0.525 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **18** was obtained in 59% (0.159 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (t, J = 8.0 Hz, 1H), 7.42-7.30 (m, 3H), 7.25-7.08 (m, 5H), 3.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (dd, J = 249.2, 7.4 Hz), 144.7, 132.4 (d, J = 2.7 Hz), 131.9 (d, J = 2.7 Hz), 131.2 (d, J = 8.1 Hz), 130.4 (d, J = 8.1 Hz), 129.3, 124.6 (d, J = 3.4 Hz), 124.4 (d, J = 3.4 Hz), 119.1 (d, J = 14.9 Hz), 118.1 (d, J = 14.9 Hz), 116.1 (d, J = 13.2 Hz), 115.9 (d, J = 13.2 Hz), 32.4. $C_{16}H_{12}F_2N_2$ (270.28): Calcd C 71.10, H 4.48, N 10.36; Found C 71.27, H 4.55, N 10.51.

1-Methyl-2,5-di*o*-tolylimidazole (19)

From 2-bromotoluene (0.513 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **19** was obtained in 54% (0.141 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.15 (m, 8H), 7.03 (s, 1H), 3.11 (s, 3H), 2.21 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 138.2, 132.4, 131.3, 130.6, 130.5, 130.4, 130.3, 129.7, 129.4, 129.0, 126.7, 125.9, 125.8, 31.5, 20.0, 19.7. $C_{18}H_{18}N_2$ (262.35): Calcd C 82.41, H 6.92, N 10.68; Found C 82.50, H 6.98, N 10.40.

3,3'-(1-Methylimidazole-2,5-diyl)dipyridine (20)

From 3-bromopyridine (0.474 g, 3 mmol), 1-methylimidazole (0.082 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **20** was obtained in 72% (0.170 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.68 (s, 1H), 8.62 (d, J = 4.6 Hz, 1H), 8.58 (d, J = 4.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.40-7.34 (m, 2H), 7.34 (s, 1H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 149.4, 149.3, 149.2, 147.1, 136.3, 135.9, 132.6, 128.9, 126.6, 125.9, 123.7, 123.6, 33.7. $C_{14}H_{12}N_4$ (236.27): Calcd C 71.17, H 5.12, N 23.71; Found C 71.08, H 5.20, N 23.49.

1-*n*-Butyl-2,5-bis(4-chlorophenyl)-imidazole (21b)

From 4-bromochlorobenzene (0.574 g, 3 mmol), 1-butylimidazole (0.124 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **21b** was obtained in 24% (0.083 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.06 (s, 1H), 3.99 (t, J = 7.5 Hz, 2H), 1.26-1.15 (m, 2H), 0.90-0.83 (m, 2H), 0.57 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 135.0, 134.2, 133.6, 130.2, 130.1, 129.9, 129.1, 128.9, 128.5, 44.9, 32.4, 19.3, 13.3. $C_{19}H_{18}Cl_2N_2$ (345.27): Calcd C 66.09, H 5.25, N 8.11; Found C 66.14, H 5.08, N 7.89. The mono-arylation product **21a** was also isolated in 45% yield (0.105 g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 6.98 (s, 1H), 3.87 (t, J = 7.5 Hz, 2H), 1.53 (quint., J = 7.5 Hz, 2H), 1.16 (sext., J = 7.5 Hz, 2H), 0.77 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 134.0, 131.7, 130.0, 129.0, 128.7, 128.3, 45.1, 32.9, 19.6, 13.4.

2,5-Bis(3,5-bis(trifluoromethyl)phenyl)-1-butylimidazole (22b)

From 3,5-bis(trifluoromethyl)bromobenzene (0.879 g, 3 mmol), 1-butylimidazole (0.124 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **22b** was obtained in 35% (0.192 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 2H), 7.91 (s, 1H), 7.88 (s, 1H), 7.84 (s, 2H), 7.26 (s, 1H), 4.04 (t, J = 7.5 Hz, 2H), 1.40-1.25 (m, 2H), 1.05-0.90 (m, 2H), 0.60 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 133.0-131.5

(m), 130.4, 128.8, 128.6, 127.1, 124.4, 122.8 (q, J = *J* = 3.7 Hz), 122.1 (q, *J* = 3.7 Hz), 121.6, 118.9, 45.4, 32.6, 19.2, 13.0. $C_{23}H_{16}F_{12}N_2$ (548.37): Calcd C 50.38, H 2.94, N 5.11; Found C 50.19, H 2.78, N 4.83. The 2,4,5-tri-arylation product **22c** was also isolated in 33% yield (0.251 g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 2H), 8.02 (s, 1H), 7.97 (s, 1H), 7.85 (s, 2H), 7.78 (s, 2H), 7.64 (s, 1H), 3.89 (t, *J* = 7.5 Hz, 2H), 1.40-1.25 (m, 2H), 1.05-0.90 (m, 2H), 0.60 (t, *J* = 7.5 Hz, 3H).

1-*n*-Butyl-2,5-di*p*-tolylimidazole (23b)

From 4-bromotoluene (0.513 g, 3 mmol), 1-butylimidazole (0.124 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **23b** was obtained in 25% (0.076 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.23-7.17 (m, 4H), 7.02 (s, 1H), 3.99 (t, *J* = 7.5 Hz, 2H), 2.34 (s, 6H), 1.26-1.15 (m, 2H), 0.90-0.83 (m, 2H), 0.54 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 138.5, 137.8, 134.3, 129.4, 129.2, 128.8, 128.7, 128.0, 127.7, 44.7, 32.3, 21.4, 21.3, 19.3, 13.3. $C_{21}H_{24}N_2$ (304.43): Calcd C 82.85, H 7.95, N 9.20; Found C 82.67, H 8.14, N 9.02. The mono-arylation product **23a** was also isolated in 31% yield (0.066 g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.20-7.16 (m, 4H), 6.95 (s, 1H), 3.87 (t, *J* = 7.5 Hz, 2H), 2.34 (s, 3H), 1.60-1.40 (m, 2H), 1.20-1.05 (m, 2H), 0.77 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 132.9, 129.4, 128.7, 127.9, 127.3, 45.0, 32.9, 21.2, 19.7, 13.5.

5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-imidazole (24a)

From 4-bromochlorobenzene (0.574 g, 3 mmol), 1-(4-methoxyphenyl)-imidazole (0.174 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **25a** was obtained in 62% (0.176 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.13 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 139.4, 133.4, 132.1, 129.3, 129.2, 128.8, 128.7, 128.0, 127.0, 114.7, 55.5. $C_{16}H_{13}ClN_2O$ (284.74): Calcd C 67.49, H 4.60, N 9.84; Found C 67.28, H 4.37, N 10.08.

5-(3,5-Bis(trifluoromethyl)phenyl)-1-(4-methoxyphenyl)-imidazole (25a)

From 3,5-bis(trifluoromethyl)bromobenzene (0.879 g, 3 mmol), 1-(4-methoxyphenyl)-imidazole (0.174 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **25a** was obtained in 75% (0.289 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.62 (s, 1H), 7.46 (s, 2H), 7.35 (s, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 140.4, 131.7 (q, *J* = 34.0 Hz), 130.4, 130.1, 128.4, 127.3 (m), 127.1, 123.0 (q, *J* = 272.7 Hz), 120.6 (m), 115.0, 55.6. $C_{18}H_{12}F_6N_2O$ (386.29): Calcd C 55.97, H 3.13, N 7.25; Found C 55.79, H 3.20, N 7.41. The di-arylation product **25b** was also isolated in low yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 2H), 7.70 (s, 1H), 7.66 (s, 1H), 7.50 (s, 1H), 7.47 (s, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 3H).

4-(5-(4-Chlorophenyl)-imidazol-1-yl)benzaldehyde (26a)

From 4-bromochlorobenzene (0.574 g, 3 mmol), 4-(1-imidazol-1-yl)benzaldehyde (0.172 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **26a** was obtained in 53% (0.149 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.70 (s, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.22 (s, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.7, 141.1, 135.6, 134.0, 131.0, 130.0, 129.4, 129.0, 127.4, 125.7. $C_{16}H_{11}ClN_2O$ (282.72): Calcd C 67.97, H 3.92, N 9.91; Found C 67.75, H 3.97, N 9.72.

4-(5-(3,5-Bis(trifluoromethyl)phenyl)-imidazol-1-yl)benzaldehyde (27a)

From 3,5-bis(trifluoromethyl)bromobenzene (0.879 g, 3 mmol), 4-(1-imidazol-1-yl)benzaldehyde (0.172 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **27a** was obtained in 52% (0.200 g) yield. Trace of diarylation product were observed by GC/MS analysis of the crude mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.77 (s, 1H), 7.70 (s, 1H), 7.47 (s, 2H), 7.40 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4, 140.4, 139.9, 136.1, 132.2 (q, *J* = 34.0 Hz), 131.4, 131.2, 131.1, 127.7 (m), 126.0, 122.4 (q, *J* = 272.7 Hz), 121.3 (m). $C_{18}H_{10}F_6N_2O$ (384.28): Calcd C 56.26, H 2.62, N 7.29; Found C 56.41, H 2.47, N 7.48.

4-(1-Benzylimidazol-5-yl)benzonitrile (28a)

From 4-bromobenzonitrile (0.546 g, 3 mmol), 1-benzylimidazole (0.158 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **28a** was obtained in 41% (0.106 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.26-7.20 (m, 3H), 7.17 (s, 1H), 6.93 (d, *J* = 8.4 Hz, 2H), 5.13 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 136.1, 134.3, 132.5, 131.7, 130.0, 129.1, 128.8, 128.3, 126.4, 118.5, 111.5, 49.1. $C_{17}H_{13}N_3$ (259.31): Calcd C 78.74, H 5.05, N 16.20; Found C 78.40, H 4.99, N 15.91.

1-Benzyl-2,5-bis(3,5-bis(trifluoromethyl)phenyl)-imidazole (29b)

From 3,5-bis(trifluoromethyl)bromobenzene (0.879 g, 3 mmol), 1-benzylimidazole (0.158 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **29b** was obtained in 32% (0.186 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 2H), 7.81 (s, 1H), 7.76 (s,

1H), 7.67 (s, 2H), 7.38 (s, 1H), 7.28-7.20 (m, 3H), 6.81 (d, J = 8.4 Hz, 2H), 5.19 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 135.8, 133.5, 132.4 (q, J = 34.0 Hz), 132.3 (q, J = 34.0 Hz), 132.2, 131.6, 130.4, 129.4, 128.7 (m), 128.5, 125.4, 122.9 (q, J = 272.7 Hz), 122.8 (m), 122.7 (q, J = 272.7 Hz), 122.0 (m), 49.3. $C_{26}H_{14}F_{12}N_2$ (582.38): Calcd C 53.62, H 2.42, N 4.81; Found C 53.60, H 2.54, N 4.88. The 2,4,5-tri-arylation product **30c** was also isolated in 34% yield (0.269 g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 2H), 7.89 (s, 1H), 7.87 (s, 1H), 7.84 (s, 2H), 7.64 (s, 1H), 7.59 (s, 2H), 7.25-7.20 (m, 3H), 6.73 6.81 (d, J = 8.4 Hz, 2H), 5.08 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 137.7, 135.2, 134.9, 133.1 (q, J = 34.0 Hz), 132.5 (q, J = 34.0 Hz), 131.1, 131.7, 131.6, 130.8 (m), 129.4, 129.0 (m), 128.7, 126.5 (m), 125.6, 123.3 (m), 122.9 (q, J = 272.7 Hz), 122.7 (q, J = 272.7 Hz), 122.5 (q, J = 272.7 Hz), 120.9 (m), 49.4

1-Benzyl-5-(4-chlorophenyl)-imidazole (30a)[10a]

From 4-bromochlorobenzene (0.574 g, 3 mmol), 1-benzylimidazole (0.158 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **30a** was obtained in 44% (0.118 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.28-7.15 (m, 5H), 7.12 (d, J = 8.4 Hz, 2H), 7.06 (s, 1H), 6.92 (d, J = 8.4 Hz, 2H), 5.06 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 136.5, 134.2, 132.3, 130.1, 129.0, 128.9, 128.6, 128.2, 128.1, 126.5, 48.8. The di-arylation product **30b** was also isolated: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.21-7.16 (m, 6H), 7.13 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 5.15 (s, 2H).

1-Benzyl-5-*p*-tolylimidazole (31a)[10a]

From 4-bromotoluene (0.513 g, 3 mmol), 1-benzylimidazole (0.158 g, 1 mmol) and CsOAc (1.303 g, 4 mmol) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), product **31a** was obtained in 31% (0.077 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.30-7.15 (m, 3H), 7.10 (s, 4H), 7.04 (s, 1H), 6.95 (d, J = 8.0 Hz, 2H), 5.06 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.0, 136.9, 133.5, 129.4, 128.9, 128.8, 128.0, 127.9, 126.8, 126.7, 48.7, 21.2. The di-arylation product **31b** was also isolated: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.4 Hz, 2H), 7.20-7.00 (m, 10H), 6.77 (d, J = 8.4 Hz, 2H), 5.17 (s, 2H), 2.26 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.0, 137.9, 134.9, 129.3, 129.2, 128.9, 128.7, 128.6, 128.2, 127.9, 127.3, 125.8, 48.4, 21.3, 21.2.

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