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Double C-H bond functionalization for the annulative π -extension of 1-arylimidazoles: A palladium-catalyzed one pot access to imidazo[1,5-*f*]phenanthridines

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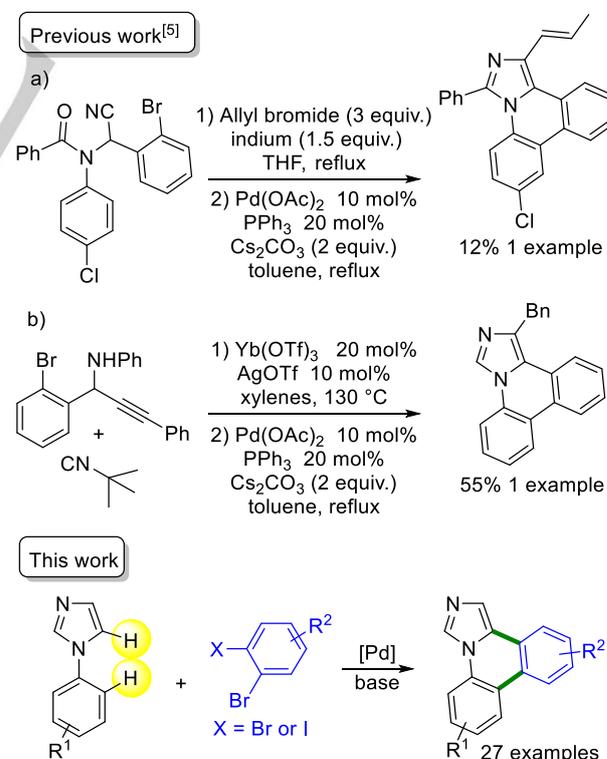
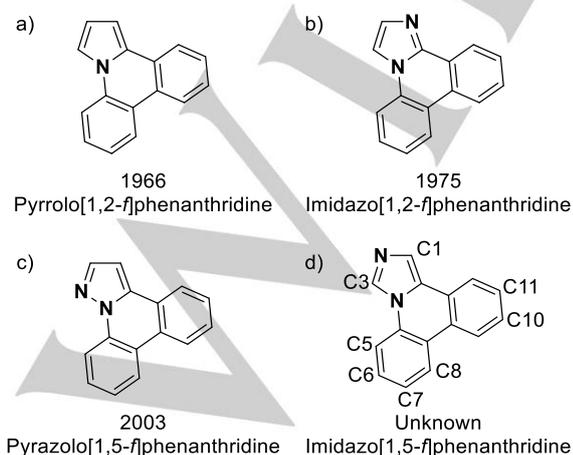
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Abstract: The Pd-catalyzed annulative π -extension reaction of 1-arylimidazoles for the one pot preparation of imidazo[1,5-*f*]phenanthridines was explored. The higher reactivity of imidazole C5-H bond compared to C2-H bond of imidazoles for Pd-catalyzed direct arylation in the presence of carboxylate bases allows the selective synthesis of imidazo[1,5-*f*]phenanthridines. The reaction proceeds *via* successive palladium-catalyzed direct intermolecular C5-arylation of the imidazole unit followed by an intramolecular direct arylation step. This synthetic pathway allowed us to describe the first synthesis of imidazo[1,5-*f*]phenanthridine. Moreover, by using the appropriate substrates, the introduction of desired functional groups at positions 5, 7, 10 and 11 of imidazo[1,5-*f*]phenanthridines is possible.

Moreover, very rare examples of compounds containing imidazo[1,5-*f*]phenanthridine structure are known.^[5] In 2010, Kim et al. prepared a single example of an imidazo[1,5-*f*]phenanthridine from a α -amino nitrile using an indium allylation reaction followed by an intramolecular Pd-catalyzed reaction (overall yield for the two steps: 12%) (Scheme 1, a).^[5a] Five year later, Zhu et al. employed *tert*-butylisocyanide and a *N*-benzyl-1,3-diarylprop-2-yl-1-amine to prepare in two steps 1-benzylimidazo[1,5-*f*]phenanthridine. Again, the reaction was limited to a single example and the overall yield of the synthesis was quite low (Scheme 1, b).^[5b] Moreover, the reactants of these two reactions are not commercially available. Therefore, the discovery of a simpler route to imidazo[1,5-*f*]phenanthridines using commercially available substrates allowing to regioselectively introduce functional groups at the desired positions is still needed.

Introduction

Polyaromatics containing heteroelements are widely used in material chemistry due to their influence on the physical properties. The introduction of the appropriate heteroelements at suitable positions allows for example to tune their photophysical properties.^[1] Many *N*-containing polyaromatics have been synthesized. For example, pyrrolo[1,2-*f*]phenanthridine has been prepared in 1966 (Fig 1, a),^[2] imidazo[1,2-*f*]phenanthridine was described in 1975 (Fig 1, b),^[3] and pyrazolo[1,5-*f*]phenanthridine in 2003 (Fig 1, c).^[4] Conversely, to the best of our knowledge, the preparation of imidazo[1,5-*f*]phenanthridine (Fig. 1, d), has not been reported.



Scheme 1. Methods for the synthesis of imidazo[1,5-*f*]phenanthridines.

Figure 1. Structures of pyrrolo-, pyrazolo- or imidazo-phenanthridines.

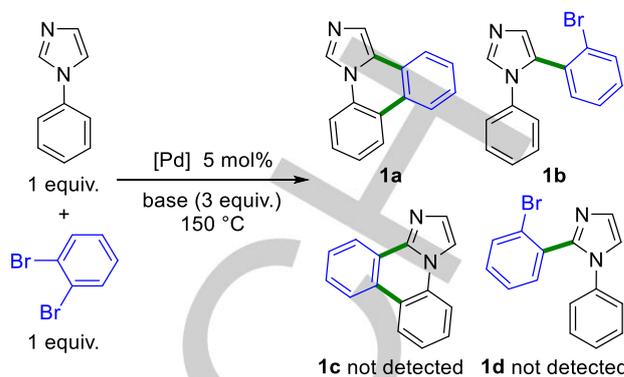
Over the past two decades, the Pd-catalyzed C–H arylation of a wide variety of (hetero)arenes led to a revolution in the preparation of poly(hetero)aryls.^[6,7] Since the seminal results of Ohta and co-workers in 1992,^[8] several groups described conditions allowing the intermolecular Pd-catalyzed direct 2- or 5-arylation of imidazoles.^[9,10] In the presence of carboxylate bases, generally very regioselective arylations at the C5-position of imidazoles were obtained; whereas the use of stronger bases allowed to arylate the C2-position. Moreover, Pd-catalyzed intramolecular C–H arylations between an aryl halide and a benzene derivative to form 5- or 6-membered rings is also well documented.^[11,12] Therefore, by combining palladium-catalyzed regioselective intermolecular C–H arylation at the C5-positions of imidazoles using a carboxylate base with an intramolecular C–H arylation, the one pot access to imidazo[1,5-*f*]phenanthridines should be possible.

Herein, we report *i*) conditions for the annulative π -extension of diversely functionalized 1-arylimidazoles by 1,2-dihalobenzenes in the presence of palladium catalysts *via* successive palladium-catalyzed direct arylations; *ii*) the first preparation of imidazo[1,5-*f*]phenanthridine; *iii*) on the functional group tolerance on both coupling partners for the introduction of substituents at desired positions.

Results and Discussion

We employed 1-phenylimidazole (1 equiv.) and 1,2-dibromobenzene (1 equiv.) as model substrates for our study (Table 1). We first determined the reaction outcome in the presence of various bases using 5 mol% Pd(OAc)₂ catalyst in DMA. This catalyst precursor associated with this solvent is often very effective for the direct coupling of 5-membered ring heteroarenes with aryl halides.^[13] Cs₂CO₃, K₂CO₃ and NaOAc were completely ineffective bases, and CsOAc or KOAc gave imidazo[1,5-*f*]phenanthridine **1a** in trace amount (Table 1, entries 1-5). By contrast, the use of KOPIv afforded **1a** in quite good selectivity but in low yield (Table 1, entry 6). The influence of the presence of four diphosphine ligands in the reaction mixture was examined. Better yields in **1a** (18% and 20%) were obtained using dppe and dppb ligands associated to Pd(OAc)₂ (entries 7 and 9); whereas dppp and dppf ligands were less effective (entries 8 and 10). The use of PdCl(C₃H₅)(dppb) catalyst allowed to increase the yield in **1a** to 28% (Table 1, entry 11).^[14] Xylene as solvent was ineffective; whereas, both DMF or NMP led to **1a** in moderate to quite good yields (Table 1, entries 12-14). Longer reaction times (48 or 72 h) allowed to slightly improve the yield in **1a** up to 52% and the selectivities; whereas the use of a lower reaction temperature decreased the yield (Table 1, entries 16-18). From 1-bromo-2-iodobenzene instead of 1,2-dibromobenzene as the aryl source, the yield in **1a** slightly decreased (Table 1, entry 19). In the course of these reactions, no formation of imidazo[1,2-*f*]phenanthridine **1c** or C2-arylated imidazole derivative **1d** was detected. The complete regioselectivity in favor of the arylation at the C5-position of the imidazole unit is probably due to a concerted metalation deprotonation mechanism which is known to favor the arylation at that position.^[15]

Table 1. Influence of the reaction conditions on the Pd-catalyzed reaction of 1-phenylimidazole with 1,2-dibromobenzene.^[a]



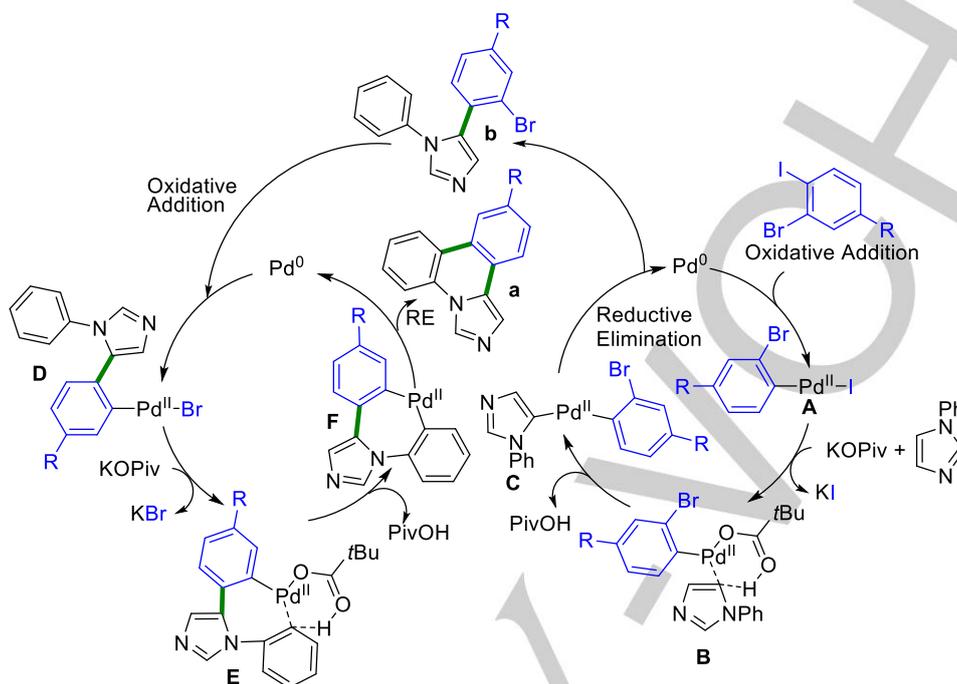
Entry	Catalyst	Solvent	Base	Time (h)	Ratio 1a : 1b	Yield in 1a (%)
1	Pd(OAc) ₂	DMA	Cs ₂ CO ₃	16	-	0
2	Pd(OAc) ₂	DMA	K ₂ CO ₃	16	-	0
3	Pd(OAc) ₂	DMA	NaOAc	16	-	0
4	Pd(OAc) ₂	DMA	CsOAc	16	-	<5
5	Pd(OAc) ₂	DMA	KOAc	16	-	<5
6	Pd(OAc) ₂	DMA	KOPIv	16	72:28	10
7	Pd(OAc) ₂ /dppe	DMA	KOPIv	16	66:34	18
8	Pd(OAc) ₂ /dppp	DMA	KOPIv	16	74:26	15
9	Pd(OAc) ₂ /dppb	DMA	KOPIv	16	75:25	20
10	Pd(OAc) ₂ /dppf	DMA	KOPIv	16	75:25	11
11	PdCl(C ₃ H ₅)(dppb)	DMA	KOPIv	16	75:25	28
12	PdCl(C ₃ H ₅)(dppb)	xylene	KOPIv	16	-	0
13	PdCl(C ₃ H ₅)(dppb)	NMP	KOPIv	16	76:24	25
14	PdCl(C ₃ H ₅)(dppb)	DMF	KOPIv	16	85:15	41
15	PdCl(C ₃ H ₅)(dppb)	DMF	KOPIv	48	87:13	47
16	PdCl(C ₃ H ₅)(dppb)	DMA	KOPIv	48	80:20	52
17	PdCl(C ₃ H ₅)(dppb)	DMA	KOPIv	72	85:15	51
18	PdCl(C ₃ H ₅)(dppb)	DMA	KOPIv	48	75:25	<10 ^[b]
19	PdCl(C ₃ H ₅)(dppb)	DMA	KOPIv	48	77:23	45 ^[c]

[a] [Pd] (0.05 equiv.), 1-phenylimidazole (1 equiv.), 1,2-dibromobenzene (1 equiv.), base (3 equiv.), 150 °C, isolated yields. [b] 130 °C. [c] From 1-bromo-2-iodobenzene.

The use of substituted 1-bromo-2-iodobenzenes should allow to regioselectively introduce a substituent at the desired position of the imidazo[1,5-*f*]phenanthridines, due to the faster oxidative addition to palladium of the C–I bond than for the C–Br bond. Therefore, first step of the catalytic cycle involves the oxidative addition of the 1-bromo-2-iodobenzenes to give intermediate **A** (Scheme 2). Then, after a concerted metalation deprotonation, the intermediate **C** is obtained. A reductive elimination gives the

intermediate 5-(2-bromoaryl)-1-arylimidazole **b**. This catalytic cycle is followed by a second one involving an oxidative addition of **b** to give intermediate **D**. Then, an intramolecular C–Br/C–H bond coupling of the two aryl rings of 5-(2-bromoaryl)-1-

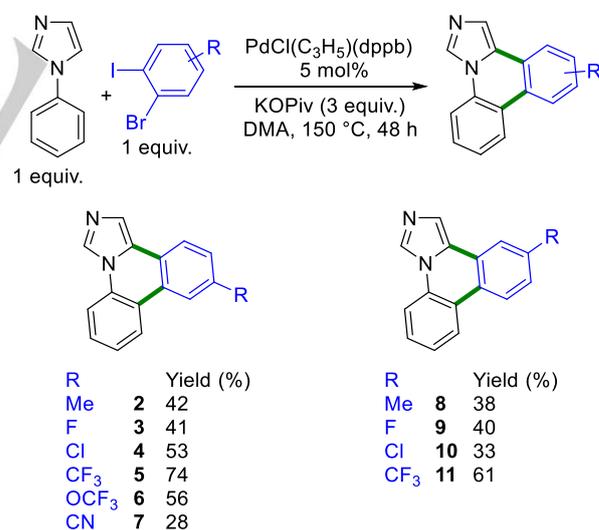
arylimidazole **b** gives the imidazo[1,5-*f*]phenanthridines **a** via the formation of intermediates **E** and **F**.



Scheme 2. Plausible mechanism.

In order to prepare C10- and C11-substituted imidazo[1,5-*f*]phenanthridines, 1-phenylimidazole was reacted with a set of 1-bromo-2-iodobenzenes in the presence of 5 mol% PdCl(C₃H₅)(dppb), KO₂Piv as the base in DMA (Scheme 3). The one pot synthesis of C10-substituted imidazo[1,5-*f*]phenanthridines from 5-substituted 1-bromo-2-iodobenzenes was first examined. 1-Bromo-2-iodobenzenes containing methyl, fluoro, chloro, trifluoromethyl, trifluoromethoxy or nitrile C5-substituents with 1-phenylimidazole led to the expected C10-substituted imidazo[1,5-*f*]phenanthridines **2-6** in 41–74% yields. In the course of the annulation with 1-bromo-5-chloro-2-iodobenzene, the C–Cl bond remained untouched potentially allowing further functionalizations. A lower yield in **7** was obtained using the more electron-deficient 3-bromo-4-iodobenzonitrile. However, the introduction of a nitrile substituent on such compounds might be very useful for further modifications.

Then, in order to obtain C11-substituted imidazo[1,5-*f*]phenanthridines, we explored the reactivity of 4-substituted 1-bromo-2-iodobenzenes (Scheme 3). Similar yields in products **8-11** than with the 5-substituted 1-bromo-2-iodobenzenes were obtained. For example, again, 1-bromo-4-chloro-2-iodobenzene was tolerated affording the C11-chloro-substituted imidazo[1,5-*f*]phenanthridine **10** in 33% yield. The reaction of 1-phenylimidazole with 1-bromo-2-iodo-4-(trifluoromethyl)benzene gave the imidazo[1,5-*f*]phenanthridine **11** in 61% yield.

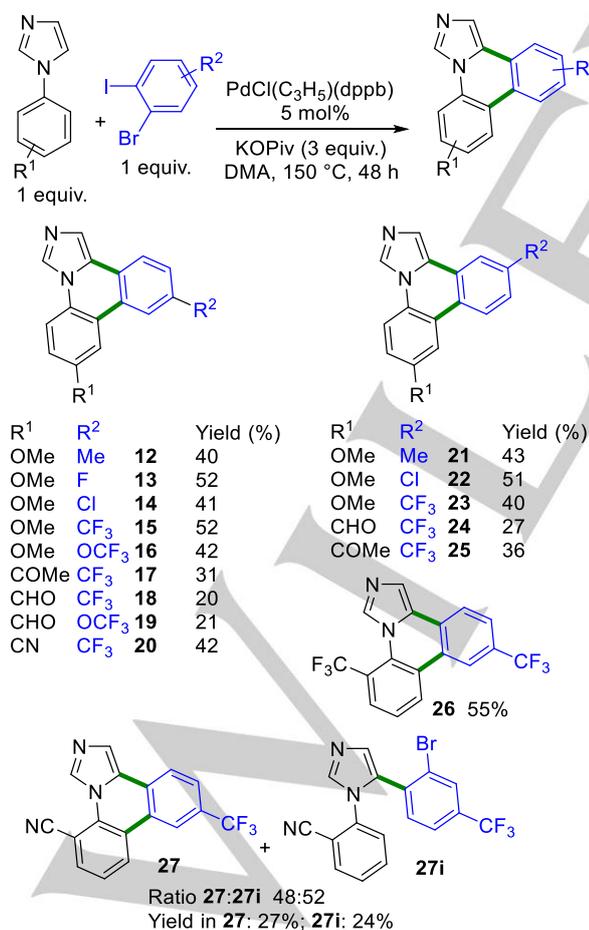


Scheme 3. Scope of the reaction with 1-bromo-2-iodobenzenes.

The influence of substituents on the aryl unit of 1-arylimidazoles was also evaluated (Scheme 4). A methoxy-*para*-substituent was well tolerated giving rise to a range of C7-methoxy-substituted imidazo[1,5-*f*]phenanthridines. For example, quite good yields in the expected 7-methoxyimidazo[1,5-*f*]phenanthridines **13**, **15** and **16** were obtained with 5-fluoro, 5-trifluoromethyl- or 5-trifluoromethoxy-substituted 1-bromo-2-

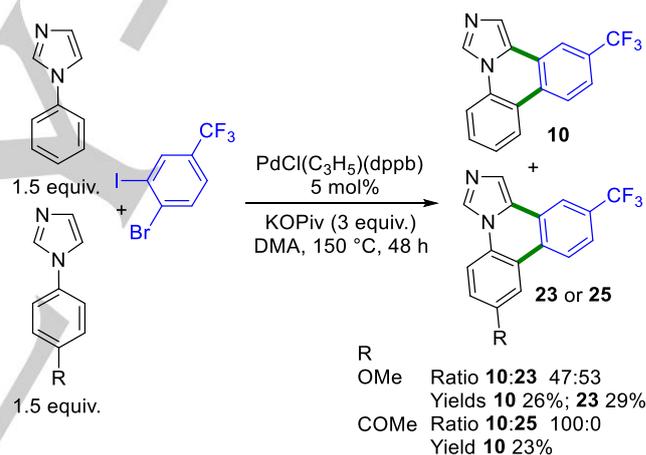
iodobenzenes. Conversely, the presence of acetyl and formyl substituents on the aryl ring of 1-arylimidazoles had a deleterious effect. From both 4-(imidazol-1-yl)acetophenone and 4-(imidazol-1-yl)benzaldehyde using 1-bromo-2-iodo-5-(trifluoromethyl)benzene as reaction partner, the desired C7,C10-substituted imidazo[1,5-*f*]phenanthridines **17** and **18** were only obtained in 31% and 20% yield, respectively. A better yield in **19** was obtained using 4-(1H-imidazol-1-yl)benzotrile as imidazole source. Then, the reactivity of a set of 1-arylimidazoles with 4-substituted 1-bromo-2-iodobenzenes was examined. 1-(4-Methoxyphenyl)imidazole reacted nicely with 1-bromo-2-iodobenzenes containing methyl, chloro or trifluoromethyl substituents at 4-position, providing the C7,C11-disubstituted imidazo[1,5-*f*]phenanthridines **21-23** in 40-51% yields. Using 4-(imidazol-1-yl)acetophenone and 1-bromo-2-iodo-4-(trifluoromethyl)benzene, the imidazo[1,5-*f*]phenanthridine **25** was obtained in 37% yield.

The reaction outcome using *ortho*-substituted 1-arylimidazoles was also explored. From a trifluoromethyl-substituted 1-arylimidazole, the annulation reaction occurred, providing the C5,C10-disubstituted imidazo[1,5-*f*]phenanthridine **26** in moderate yield. By contrast, in the presence of 2-(1H-imidazol-1-yl)benzotrile, a mixture of the imidazo[1,5-*f*]phenanthridine **27** and the uncyclized intermediate product **27i** was obtained in a 48:52 ratio indicating that with this imidazole derivative, the intramolecular C-H activation step is more challenging.



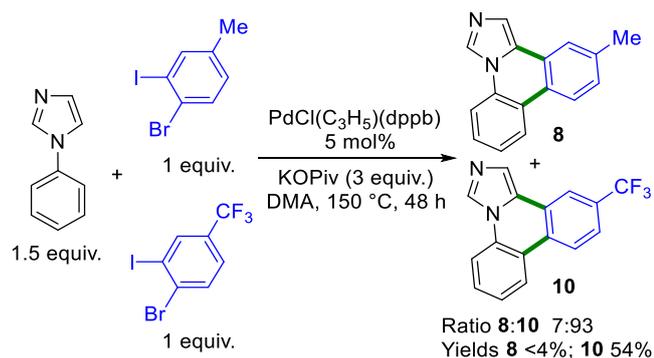
Scheme 4. Scope of the reaction with substituted 1-arylimidazoles.

To determine the influence of the substituents on both coupling partners, we performed competition reactions (Schemes 5 and 6). From an equimolar mixture of 1-phenylimidazole and 1-(4-methoxyphenyl)imidazole with 1-bromo-2-iodo-4-(trifluoromethyl)benzene as reaction partner, we observed the formation of an almost equimolar mixture of the imidazo[1,5-*f*]phenanthridines **10** and **23** (ratio **10**:**23** 47:53). At the end of the reaction, a 70% conversion of 1-bromo-2-iodo-4-(trifluoromethyl)benzene was observed. A very different result was observed using 1-phenylimidazole and 1-(4-(imidazol-1-yl)phenyl)ethan-1-one, with the exclusive formation of **10** in only 23% yield due to a poor conversion of the reactants. The presence of 1-(4-(imidazol-1-yl)phenyl)ethan-1-one in the reaction mixture seems to partially poison the catalyst. These results and also those of scheme 4 indicate that the presence of an electron-withdrawing substituent on the aryl ring of 1-arylimidazole has a deleterious effect. This result is consistent with the results observed by Fagnou et al. on the intramolecular arylation of 2-bromobenzamides bearing methoxy or nitro substituents for which the less reactive arene was the most electron-deficient.¹⁶ With electron-deficient aryl rings on the 1-arylimidazoles, the formation of the Pd-intermediate **E** of the scheme 2 appears to be slower.



Scheme 5. Competition reactions to probe the substitution preference.

Finally, a competition reaction using an equimolar mixture of the 1-bromo-2-iodobenzenes bearing 4-methyl- or 4-trifluoromethyl-substituents with 1-phenylimidazole (1.5 equiv.) afforded a mixture of the products **8** and **10** in 7:93 ratio and <4%:54% yields. This result is consistent with a faster oxidative addition of 1-bromo-2-iodo-4-(trifluoromethyl)benzene than 1-bromo-2-iodo-4-methylbenzene to palladium to form the Pd-intermediate **A** of the scheme 2. At the end of the reaction, a very large amount of 1-bromo-2-iodo-4-methylbenzene and also a significant amount of 1-phenyl-1H-imidazole was recovered unreacted.



Scheme 6. Competition reactions to probe the substitution preference.

Conclusion

In summary, we report herein the first synthesis of imidazo[1,5-*f*]phenanthridine and the first general method for the synthesis of imidazo[1,5-*f*]phenanthridine derivatives. Our method employs a Pd-catalyzed intermolecular associated to an intramolecular double C–H bond arylation of 1-arylimidazoles. This procedure tolerates several useful substituents on the 1-arylimidazole and on aryl dihalide such as methoxy, fluoro, chloro, formyl, acetyl or nitrile. With this synthetic pathway, by using the appropriate substrates the introduction of desired functional groups at positions 5, 7, 10 and 11 of imidazo[1,5-*f*]phenanthridines is possible. Moreover, our procedure uses easily available substrates and an air-stable catalyst associated to KOPiv as inexpensive base. This inedited synthetic scheme which employs very simple reaction conditions should be attractive to chemists looking for easy routes to functionalized imidazo[1,5-*f*]phenanthridines.

Experimental Section

General procedure for palladium-catalyzed synthesis of imidazo[1,5-*f*]phenanthridines:

The reaction of the aryl dihalide (1 mmol), 1-arylimidazole (1 mmol) and KOPiv (0.420 g, 3 mmol) in the presence of PdCl₂(C₃H₅)₂(dppb) (30.5 mg, 0.05 mmol) at 150 °C during 48 h in DMA (4 mL) under argon affords the coupling products **1a** and **2-27** after evaporation of the solvent and purification on silica gel. Eluent MeOH/EtOAc/heptane: 3/6/91 for compounds **1a**, **2-26**. MeOH/EtOAc/heptane: 1/2/97 for compounds **27** and **27i**. Some of these products were not very stable at room temperature and were stored in a fridge, and for some of them their solubility was low in CDCl₃.

Imidazo[1,5-*f*]phenanthridine (**1a**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 1,2-dibromobenzene (0.236 g, 1 mmol), product **1a** was obtained in 56% yield (0.122 g) as a yellow solid: mp 104–106 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.58 (s, 1H), 8.34 (dd, *J* = 8.1, 1.4 Hz, 1H), 8.25 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.94 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.83 (s, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.54–7.45 (m, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 130.9, 129.4, 129.1, 128.8, 127.7, 127.5, 125.9, 125.6, 124.5, 124.4, 123.4, 122.9, 122.6, 122.5, 115.5. HRMS calcd for [M+H]⁺ C₁₅H₁₁N₂ 219.0917, found: 219.0917.

10-Methylimidazo[1,5-*f*]phenanthridine (**2**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 2-bromo-1-iodo-4-methylbenzene (0.297 g, 1 mmol), product **2** was obtained in 42% yield (0.097 g) as a yellow solid: mp 160–162 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.55 (s, 1H), 8.34 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.05 (s, 1H), 7.96–7.89 (m, 2H), 7.78 (s, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.6 Hz, 1H), 2.53 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 137.3, 131.0, 130.0, 129.0, 128.9, 127.8, 125.8, 125.5, 124.3, 123.3, 123.0, 122.5, 122.0, 121.8, 115.4, 22.2. HRMS calcd for [M+H]⁺ C₁₆H₁₃N₂ 233.1073, found: 233.1073.

10-Fluoroimidazo[1,5-*f*]phenanthridine (**3**)

From 1-phenylimidazole 0.144 g, 1 mmol) and 2-bromo-4-fluoro-1-iodobenzene (0.301 g, 1 mmol), product **3** was obtained in 41% yield (0.097 g) as a white solid: mp 208–210 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.50 (s, 1H), 8.12 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.90 (dd, *J* = 9.0, 5.3 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.78 (dd, *J* = 10.4, 2.6 Hz, 1H), 7.71 (s, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.20 (td, *J* = 8.4, 2.5 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 162.1 (d, *J* = 246.1 Hz), 131.0, 129.7, 129.1, 127.4 (d, *J* = 8.1 Hz), 127.1, 125.9, 125.3 (d, *J* = 8.5 Hz), 124.5, 122.0, 121.6 (d, *J* = 3.1 Hz), 120.5 (d, *J* = 2.5 Hz), 116.8 (d, *J* = 23.2 Hz), 115.5, 109.0 (d, *J* = 23.5 Hz). HRMS calcd for [M+H]⁺ C₁₅H₉FN₂ 237.0823, found: 237.0825.

10-Chloroimidazo[1,5-*f*]phenanthridine (**4**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 2-bromo-4-chloro-1-iodobenzene (0.317 g, 1 mmol), product **4** was obtained in 53% yield (0.134 g) as a yellow solid: mp 188–190 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.52 (bs, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.76 (bs, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.51–7.33 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 133.2, 130.9, 129.9, 129.6, 128.8, 127.5, 126.8, 125.9, 124.5, 124.2, 122.7, 121.5, 121.2, 115.4. HRMS calcd for [M+H]⁺ C₁₅H₁₀ClN₂ 253.0527, found: 253.0530.

10-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridine (**5**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **5** was obtained in 74% yield (0.212 g) as a yellow solid: mp 192–194 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.62 (s, 1H), 8.47 (s, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.92 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 130.9, 129.9, 129.1 (q, *J* = 33.0 Hz), 126.9, 126.2, 125.5, 125.0 (q, *J* = 3.5 Hz), 124.4, 124.2 (q, *J* = 272.5 Hz), 124.1, 123.8, 121.4, 120.1 (q, *J* = 4.0 Hz), 115.5. HRMS calcd for [M+H]⁺ C₁₆H₁₀F₃N₂ 287.0791, found: 287.0788.

10-(Trifluoromethoxy)imidazo[1,5-*f*]phenanthridine (**6**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethoxy)benzene (0.367 g, 1 mmol), product **6** was obtained in 56% yield (0.169 g) as a yellow solid: mp 152–154 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.56 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.02 (s, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.81 (s, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 148.3 (q, *J* = 2.3 Hz), 130.9, 129.8, 129.5, 127.0, 126.6, 126.0, 124.9, 124.4, 123.0, 122.8, 121.6, 121.3, 120.5 (q, *J* = 258.0 Hz), 115.5, 115.2. HRMS calcd for [M+H]⁺ C₁₆H₁₀F₃N₂O 303.0740, found: 303.0735.

Imidazo[1,5-*f*]phenanthridine-10-carbonitrile (**7**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 3-bromo-4-iodobenzonitrile (0.308 g, 1 mmol), product **7** was obtained 28% yield (0.068 g) as a yellow solid: mp 248-250 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.64 (bs, 1H), 8.50 (d, *J* = 1.5 Hz, 1H), 8.28 (d, *J* = 8.3 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 8.00-7.94 (m, 2H), 7.73 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 131.2, 131.1, 130.5, 127.7, 127.6, 126.6, 126.0, 125.9, 125.2, 124.5, 124.1, 120.8, 118.9, 115.7, 112.2, 110.8. HRMS calcd for [M+H]⁺ C₁₆H₁₀N 244.0869, found: 244.0869.

11-Methylimidazo[1,5-*f*]phenanthridine (**8**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 1-bromo-2-iodo-4-methylbenzene (0.297 g, 1 mmol), product **8** was obtained in 38% yield (0.088 g) as a yellow solid: mp 156-158 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.56 (bs, 1H), 8.29 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 7.92 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.80 (s, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 8.3, 1.8 Hz, 1H), 2.50 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 138.9, 130.6, 129.3, 128.9, 128.6, 127.7, 125.8, 124.4, 124.2, 123.4, 123.1, 122.8, 122.7, 122.4, 115.4, 21.6. HRMS calcd for [M+H]⁺ C₁₆H₁₃N₂ 233.1073, found: 233.1076.

11-Fluoroimidazo[1,5-*f*]phenanthridine (**9**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 1-bromo-4-fluoro-2-iodobenzene (0.301 g, 1 mmol), product **9** was obtained in 40% yield (0.094 g) as a white solid: mp 212-214 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.59 (s, 1H), 8.27 (d, *J* = 8.2 Hz, 1H), 8.22 (dd, *J* = 9.0, 5.3 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.82 (s, 1H), 7.64 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.20 (td, *J* = 8.8, 2.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 162.7 (d, *J* = 248.6 Hz), 130.3, 129.6, 128.8, 126.0, 125.1 (d, *J* = 8.9 Hz), 124.1, 123.3, 121.8, 115.4, 115.3 (d, *J* = 22.2 Hz), 109.0 (d, *J* = 23.1 Hz). HRMS calcd for [M+H]⁺ C₁₅H₉FN₂ 237.0823, found: 237.0826.

11-Chloroimidazo[1,5-*f*]phenanthridine (**10**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 2-bromo-5-chloro-1-iodobenzene (0.317 g, 1 mmol), product **10** was obtained in 33% yield (0.083 g) as a yellow solid: mp 176-178 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.60 (bs, 1H), 8.24 (d, *J* = 8.2 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 7.95-7.90 (m, 2H), 7.81 (bs, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.42 (dd, *J* = 8.7, 2.1 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 134.8, 130.7, 130.2, 129.4, 127.8, 126.2, 125.7, 124.5, 124.3, 124.0, 123.1, 122.9, 121.9, 121.8, 115.6. HRMS calcd for [M+H]⁺ C₁₅H₁₀ClN₂ 253.0527, found: 253.0525.

11-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridine (**11**)

From 1-phenylimidazole (0.144 g, 1 mmol) and 1-bromo-2-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **11** was obtained in 61% yield (0.174 g) as a white solid: mp 192-194 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.56 (s, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 8.17 (s, 1H), 7.92 (d, *J* = 7.4 Hz, 1H), 7.86 (s, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 131.2, 130.5 (q, *J* = 33.0 Hz), 130.1, 129.7, 128.0, 126.6, 126.1, 124.7, 124.4, 123.8 (q, *J* = 272.5 Hz), 123.5, 123.4 (m), 121.2, 120.3 (q, *J* = 4.0 Hz), 115.5. HRMS calcd for [M+H]⁺ C₁₆H₁₀F₃N₂ 287.0791, found: 287.0792.

7-Methoxy-10-methylimidazo[1,5-*f*]phenanthridine (**12**)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 2-bromo-1-iodo-4-methylbenzene (0.297 g, 1 mmol), product **12** was obtained in 40% yield (0.105 g) as a yellow solid: mp 198-200 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.49 (s, 1H), 7.97 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.76 (s, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.13 (dd, *J* =

8.0, 2.5 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 157.5, 137.2, 130.2, 128.6, 125.4, 125.3, 123.8, 123.4, 123.0, 122.3, 121.7, 116.7, 115.9, 107.9, 102.8, 55.9, 22.0. HRMS calcd for [M+H]⁺ C₁₇H₁₅N₂O 263.1179, found: 263.1181.

10-Fluoro-7-methoxyimidazo[1,5-*f*]phenanthridine (**13**)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 1-bromo-4-fluoro-2-iodobenzene (0.301 g, 1 mmol), product **13** was obtained in 52% yield (0.138 g) as a yellow solid: mp 176-178 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.45 (s, 1H), 7.98 (dd, *J* = 9.0, 5.3 Hz, 1H), 7.88-7.82 (m, 2H), 7.72 (s, 1H), 7.61 (d, *J* = 2.6 Hz, 1H), 7.26 (td, *J* = 8.4, 2.4 Hz, 1H), 7.19 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.96 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 162.0 (d, *J* = 246.2 Hz), 157.6, 128.8, 127.4 (d, *J* = 8.0 Hz), 120.8, 125.4 (d, *J* = 8.4 Hz), 125.3, 123.0, 121.9, 121.2, 117.1, 116.8 (m), 109.1 (d, *J* = 23.3 Hz), 108.0, 55.9. HRMS calcd for [M+H]⁺ C₁₆H₁₂FN₂O 267.0928, found: 267.0928.

10-Chloro-7-methoxyimidazo[1,5-*f*]phenanthridine (**14**)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 2-bromo-4-chloro-1-iodobenzene (0.317 g, 1 mmol), product **14** was obtained in 41% yield (0.116 g) as a yellow solid: mp 138-140 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.46 (bs, 1H), 8.06 (d, *J* = 2.0 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.76 (s, 1H), 7.66 (d, *J* = 2.7 Hz, 1H), 7.46 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.14 (dd, *J* = 9.0, 2.7 Hz, 1H), 3.97 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 157.7, 133.2, 129.1, 126.9, 125.2, 124.8, 123.3, 123.1, 122.8, 122.6, 117.0, 116.8, 107.7, 55.9. HRMS calcd for [M+H]⁺ C₁₆H₁₂ClN₂O 283.0633, found: 283.0631.

7-Methoxy-10-(trifluoromethyl)imidazo[1,5-*f*]phenanthridine (**15**)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **15** was obtained in 52% yield (0.164 g) as a yellow solid: mp 122-124 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.47 (s, 1H), 8.29 (s, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.84 (s, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.63 (d, *J* = 2.6 Hz, 1H), 7.15 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.97 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 129.4, 129.0 (q, *J* = 33.0 Hz), 127.1, 126.1, 125.2, 125.0 (m), 124.1 (q, *J* = 272.5 Hz), 123.8, 123.7, 123.2, 122.5, 119.9 (q, *J* = 4.0 Hz), 116.9, 116.6, 114.9, 107.6, 56.0. HRMS calcd for [M+H]⁺ C₁₇H₁₂F₃N₂O 317.0896, found: 317.0897.

7-Methoxy-10-(trifluoromethoxy)imidazo[1,5-*f*]phenanthridine (**16**)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethoxy)benzene (0.367 g, 1 mmol), product **16** was obtained 42% yield (0.139 g) as a white solid: mp 166-168 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.52 (s, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.97 (s, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 7.82 (s, 1H), 7.65 (d, *J* = 2.7 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.20 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.99 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 157.6, 148.1 (q, *J* = 2.1 Hz), 129.1, 126.8, 126.4, 125.1, 125.0, 123.3, 122.7, 122.6, 121.8, 120.2 (q, *J* = 258.0 Hz), 116.9, 116.7, 115.3, 107.8, 55.9. HRMS calcd for [M+H]⁺ C₁₇H₁₂F₃N₂O₂ 333.0845, found: 333.0849.

1-(10-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridin-7-yl)ethan-1-one (**17**)

From 1-(4-(imidazol-1-yl)phenyl)ethan-1-one (0.183 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **17** was obtained in 31% yield (0.102 g) as a yellow solid: mp 206-208 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.92 (s, 1H), 8.63 (s, 1H), 8.53 (s, 1H), 8.19 (dd, *J* = 8.6, 1.9 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.93 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 2.77 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 134.6, 133.8, 130.5, 129.7, 129.6 (q, *J* = 33.0 Hz), 127.0, 126.6, 125.7 (q, *J* = 3.6 Hz), 125.1, 124.9, 124.6, 124.0 (q, *J* =

272.5 Hz), 123.9, 121.6, 120.3 (q, $J = 4.0$ Hz), 115.7, 26.9. HRMS calcd for $[M+H]^+$ $C_{18}H_{12}F_3N_2O$ 329.0896, found: 329.0891.

10-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridine-7-carbaldehyde (18)

From 4-(imidazol-1-yl)benzaldehyde (0.172 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **18** was obtained in 20% yield (0.063 g) as a white solid: mp 234-236 °C. 1H NMR (400 MHz, $CDCl_3$): δ 10.20 (s, 1H), 8.86 (s, 1H), 8.68 (s, 1H), 8.57 (s, 1H), 8.20-8.10 (m, 3H), 7.97 (s, 1H), 7.81 (dd, $J = 8.4, 1.7$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 171.3, 134.9, 134.0, 130.6, 129.9 (q, $J = 32.0$ Hz), 127.2, 126.9, 126.1 (q, $J = 3.6$ Hz), 124.2, 125.0, 124.9, 124.0 (q, $J = 272.5$ Hz), 122.3, 120.6 (q, $J = 4.0$ Hz), 116.6. HRMS calcd for $[M+H]^+$ $C_{17}H_{10}F_3NO$ 315.0740, found: 315.0738.

10-(Trifluoromethoxy)imidazo[1,5-*f*]phenanthridine-7-carbaldehyde (19)

From 4-(imidazol-1-yl)benzaldehyde (0.172 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethoxy)benzene (0.367 g, 1 mmol), product **19** was obtained in 21% yield (0.069 g) as a yellow solid: mp 210-212 °C. 1H NMR (400 MHz, $CDCl_3$): δ 10.17 (s, 1H), 8.73 (s, 1H), 8.64 (s, 1H), 8.16-8.03 (m, 4H), 7.86 (s, 1H), 7.46 (d, $J = 8.6$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 148.7 (q, $J = 2.3$ Hz), 134.9, 133.9, 130.5, 130.4, 126.5, 125.5, 125.3, 123.6, 123.3, 122.8, 122.2, 120.7 (q, $J = 258.0$ Hz), 116.5, 115.7. HRMS calcd for $[M+H]^+$ $C_{17}H_{10}F_3N_2O_2$ 331.0689, found: 331.0690.

10-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridine-7-carbonitrile (20)

From 4-(1H-imidazol-1-yl)benzotrile (0.169 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **20** was obtained in 42% yield (0.131 g) as a white solid: mp 254-256 °C. 1H NMR (400 MHz, $CDCl_3$): δ 9.37 (d, $J = 1.7$ Hz, 1H), 9.25 (s, 1H), 8.98 (s, 1H), 8.57 (d, $J = 8.6$ Hz, 1H), 8.40 (d, $J = 8.3$ Hz, 1H), 8.18 (s, 1H), 8.16 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.96 (d, $J = 8.4$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.4, 133.2, 132.7, 130.4, 128.0 (q, $J = 32.0$ Hz), 127.1, 125.7, 125.9 (q, $J = 3.6$ Hz), 125.7, 125.1, 124.4, 124.2, 123.0 (q, $J = 272.5$ Hz), 121.6 (m), 120.6, 118.4, 109.0. HRMS calcd for $[M+H]^+$ $C_{17}H_9F_3N_3$ 312.0743, found: 312.0744.

7-Methoxy-11-methylimidazo[1,5-*f*]phenanthridine (21)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 1-bromo-2-iodo-4-methylbenzene (0.297 g, 1 mmol), product **21** was obtained in 43% yield (0.113 g) as a white solid: mp 88-90 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.49 (s, 1H), 8.07 (d, $J = 8.3$ Hz, 1H), 7.85 (d, $J = 9.0$ Hz, 1H), 7.81 (s, 1H), 7.79 (s, 1H), 7.74 (d, $J = 2.7$ Hz, 1H), 7.30 (d, $J = 8.3$ Hz, 1H), 7.11 (dd, $J = 8.9, 2.8$ Hz, 1H), 3.96 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 139.0, 128.9, 128.7, 127.4, 124.9, 124.7, 123.9, 123.4, 122.9, 122.8, 122.2, 116.5, 115.5, 107.7, 55.8, 21.6. HRMS calcd for $[M+H]^+$ $C_{17}H_{15}N_2O$ 263.1179, found: 263.1183.

11-Chloro-7-methoxyimidazo[1,5-*f*]phenanthridine (22)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 1-bromo-4-chloro-2-iodobenzene (0.317 g, 1 mmol), product **22** was obtained in 51% yield (0.144 g) as a white solid: mp 192-194 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.48 (bs, 1H), 8.06 (d, $J = 8.6$ Hz, 1H), 7.93 (d, $J = 2.1$ Hz, 1H), 7.83 (d, $J = 9.0$ Hz, 1H), 7.79 (s, 1H), 7.66 (d, $J = 2.5$ Hz, 1H), 7.40 (dd, $J = 8.7, 2.1$ Hz, 1H), 7.14 (dd, $J = 9.0, 2.5$ Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 134.8, 127.4, 125.9, 124.9, 124.4, 123.7, 123.1, 122.9, 122.8, 116.6, 116.2, 107.8, 55.9. HRMS calcd for $[M+H]^+$ $C_{16}H_{12}ClN_2O$ 283.0633, found: 283.0637.

7-Methoxy-11-(trifluoromethyl)imidazo[1,5-*f*]phenanthridine (23)

From 1-(4-methoxyphenyl)imidazole (0.174 g, 1 mmol) and 1-bromo-2-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **23** was obtained in 40% yield (0.126 g) as a white solid: mp 198-200 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.20 (d, $J = 8.5$ Hz, 1H), 8.17 (s, 1H), 7.84 (s, 1H), 7.83 (d, $J = 8.5$ Hz, 1H), 7.69 (d, $J = 2.6$ Hz, 1H), 7.65 (d, $J = 8.4$ Hz, 1H), 7.18 (dd, $J = 9.0, 2.6$ Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.6 (q, $J = 33.0$ Hz), 129.3, 127.8, 126.2, 125.3, 124.7, 123.8 (q, $J = 272.5$ Hz), 123.5, 123.4, 123.3, 122.4, 120.3 (q, $J = 4.0$ Hz), 117.0, 116.6, 108.2, 55.9. HRMS calcd for $[M+H]^+$ $C_{17}H_{12}F_3N_2O$ 317.0896, found: 317.0897.

11-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridine-7-carbaldehyde (24)

From 4-(imidazol-1-yl)benzaldehyde (0.172 g, 1 mmol) and 1-bromo-2-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **24** was obtained in 27% yield (0.085 g) as a yellow solid: mp 264-266 °C. 1H NMR (400 MHz, $CDCl_3$): δ 10.18 (s, 1H), 8.86 (s, 1H), 8.67 (s, 1H), 8.45 (d, $J = 8.5$ Hz, 1H), 8.25 (s, 1H), 8.15 (d, $J = 8.5$ Hz, 1H), 8.12 (d, $J = 8.5$ Hz, 1H), 7.95 (s, 1H), 7.76 (d, $J = 8.3$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.4, 135.0, 133.8, 131.5 (q, $J = 33.0$ Hz), 130.8, 130.5, 127.3, 126.9, 125.0, 124.7, 124.1, 124.0 (q, $J = 3.6$ Hz), 123.8, 123.6 (q, $J = 272.5$ Hz), 121.9, 120.5 (q, $J = 4.0$ Hz), 116.4. HRMS calcd for $[M+H]^+$ $C_{17}H_{10}F_3NO$ 315.0740, found: 315.0736.

1-(11-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridin-7-yl)ethan-1-one (25)

From 1-(4-(imidazol-1-yl)phenyl)ethan-1-one (0.183 g, 1 mmol) and 1-bromo-2-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **25** was obtained in 36% yield (0.118 g) as a yellow solid: mp 222-224 °C. 1H NMR (400 MHz, $CD_2Cl_2 + CDCl_3$): δ 8.86 (s, 1H), 8.56 (s, 1H), 8.37 (d, $J = 8.5$ Hz, 1H), 8.15 (s, 1H), 8.13 (d, $J = 8.5$ Hz, 1H), 7.95 (d, $J = 8.5$ Hz, 1H), 7.84 (s, 1H), 7.68 (d, $J = 8.3$ Hz, 1H), 2.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.3, 134.5, 134.0, 131.0 (q, $J = 33.0$ Hz), 130.4, 130.0, 127.7, 126.7, 125.2, 124.6, 128.8 (m), 123.6 (q, $J = 272.5$ Hz), 121.3, 120.4 (q, $J = 4.0$ Hz), 115.8, 26.6. HRMS calcd for $[M+H]^+$ $C_{18}H_{12}F_3N_2O$ 329.0896, found: 329.0897.

5,10-Bis(trifluoromethyl)imidazo[1,5-*f*]phenanthridine (26)

From 1-(2-(trifluoromethyl)phenyl)-1H-imidazole (0.212 g, 1 mmol) and 1-bromo-2-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), product **26** was obtained in 55% yield (0.195 g) as a white solid: mp 228-230 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.85 (s, 1H), 8.61 (d, $J = 8.1$ Hz, 1H), 8.44 (s, 1H), 8.11 (d, $J = 8.1$ Hz, 1H), 8.03 (d, $J = 8.1$ Hz, 1H), 7.95 (s, 1H), 7.77 (d, $J = 8.3$ Hz, 1H), 7.63 (t, $J = 8.2$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 129.6 (q, $J = 33.0$ Hz), 129.5, 129.2 (q, $J = 7.2$ Hz), 128.8, 127.3, 126.0 (q, $J = 3.5$ Hz), 125.6, 125.5, 125.4, 124.9, 124.6, 124.1, 123.6, 121.5 (q, $J = 272.5$ Hz), 121.4 (q, $J = 272.5$ Hz), 120.6 (q, $J = 4.1$ Hz), 119.4 (q, $J = 32.0$ Hz). HRMS calcd for $[M+H]^+$ $C_{17}H_9F_6N_2$ 355.0664, found: 355.0669.

10-(Trifluoromethyl)imidazo[1,5-*f*]phenanthridine-5-carbonitrile (27) and 2-(5-(2-Bromo-4-(trifluoromethyl)phenyl)imidazol-1-yl)benzonitrile (27i)

From 2-(1H-imidazol-1-yl)benzotrile (0.169 g, 1 mmol) and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.351 g, 1 mmol), products **27** and **27i** were obtained in 48:52 ratio. **27** was obtained in 27% yield (0.084 g) as a white solid: mp 230-232 °C. **27i** was obtained in 24% yield (0.094 g) as a yellow solid: mp 52-54 °C.

27: 1H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.65 (d, $J = 8.3$ Hz, 1H), 8.47 (s, 1H), 8.15 (d, $J = 8.3$ Hz, 1H), 8.04 (s, 1H), 7.99 (d, $J = 7.7$ Hz, 1H), 7.82 (d, $J = 8.3$ Hz, 1H), 7.64 (t, $J = 7.9$ Hz, 1H). HRMS calcd for $[M+H]^+$ $C_{17}H_9F_3N_3$ 312.0743, found: 312.0745.

27i: ^1H NMR (400 MHz, CDCl_3): δ 7.87 (s, 1H), 7.79 (s, 1H), 7.75 (dd, $J = 8.0, 1.7$ Hz, 1H), 7.59 (td, $J = 7.8, 1.7$ Hz, 1H), 7.55–7.42 (m, 3H), 7.37 (s, 1H), 7.22 (d, $J = 8.0, 1.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.0, 138.2, 134.3, 133.9, 133.5, 132.5 (q, $J = 32.5$ Hz), 131.6, 130.9, 130.3 (q, $J = 3.5$ Hz), 129.4, 128.2, 125.2, 124.3 (q, $J = 3.5$ Hz), 123.0 (q, $J = 273.2$ Hz), 115.7, 110.9. HRMS calcd for $[\text{M}+\text{H}]^+$ $\text{C}_{17}\text{H}_{10}^{79}\text{BrF}_3\text{N}_3$ 392.0005, found: 392.0005.

Supporting information

Data available in article supplementary material.

Acknowledgements

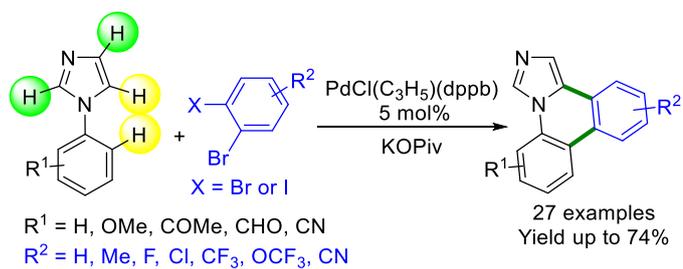
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Keywords: Catalysis • C-H bond functionalization • Direct arylation • Imidazo[1,5-f]phenanthridines • Palladium

- [1] For selected reviews, see: a) M. Bendikov, F. Wudl, D. F. Perepichka, *Chem. Rev.* **2004**, *104*, 4891–4946; b) J. E. Anthony, *Angew. Chem., Int. Ed.* **2008**, *47*, 452–483; c) C. Wang, H. Dong, W. Hu, Y. Liu, D. Zhu, *Chem. Rev.* **2012**, *112*, 2208–2267; d) W.-C. Chen, Z.-L. Zhu, C.-S. Lee, *Adv. Optical. Mater.* **2018**, *6*, 1800258; e) S. Ye, S. Zhuang, B. Pan, R. Guo, L. Wang, *J. Inf. Disp.* **2020**, *21*, 173–196; f) A. Riss, M. Richter, A. P. Paz, X.-Y. Wang, R. Raju, Y. He, J. Ducke, E. Corral, M. Wuttke, K. Seufert, M. Garnica, A. Rubio, J. V. Barth, A. Narita, K. Müllen, R. Berger, X. Feng, C.-A. Palma, W. Auwärter, *Nat. Commun.* **2020**, *11*, 1490.
- [2] R. M. Acheson, A. S. Bailey, I. A. Selby, *Chem. Commun.* **1966**, 835.
- [3] R. F. Cookson, R. E. Rodway, *J. Chem. Soc., Perkin Trans. 1* **1975**, 1850–1854.
- [4] S. Hernandez, R. SanMartin, I. Tellitu, E. Dominguez, *Org. Lett.* **2003**, *5*, 1095–1098.
- [5] For the very rare examples of preparation of imidazo[1,5-f]phenanthridines: a) Y. M. Kim, S. Lee, S. H. Kim, K. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2010**, *51*, 5922–5926; b) S. Tong, Q. Wang, M.-X. Wang, J. Zhu, *Angew. Chem., Int. Ed.* **2015**, *54*, 1293–1297. See also for the synthesis of tribenzo[*b,g,i*]imidazo[2,1,5-*de*]quinolizines: c) Q.-Q. Li, K. Ochiai, C.-A. Lee, S. Ito, *Org. Lett.* **2020**, *22*, 6132–6137; see also: d) J.-E. Yang, WO2018143663 A1 2018; e) S. Ito, Q. Li, K. Ochiai, K. Kawakami, M. Kobayashi, JP2021172623 A 2021.
- [6] For reviews on metal-catalyzed C–H bond functionalization: a) T. Satoh, M. Miura, *Chem. Lett.* **2007**, *36*, 200–205; b) L. Ackermann, R. Vicente, A. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826; c) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; d) G. P. Chiusoli, M. Catellani, M. Costa, E. Motti, N. Della Ca, G. Maestri, *Coord. Chem. Rev.* **2010**, *254*, 456–469; e) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236–10254; f) R. Rossi, F. Bellina, M. Lessi, C. Manzini, *Adv. Synth. Catal.* **2014**, *356*, 17–117; g) S. Agasti, A. Dey, D. Maiti, *Chem. Commun.* **2017**, *53*, 6544–6556; h) T. Gensch, M. J. James, T. Dalton, F. Glorius, *Angew. Chem. Int. Ed.* **2018**, *57*, 2296–2306; i) J. Kalepu, P. Gandeepan, L. Ackermann, L. T. Pilarski, *Chem. Sci.* **2018**, *9*, 4203–4216; j) S. Mao, H. Li, X. Shi, J.-F. Soule, H. Doucet, *ChemCatChem* **2019**, *11*, 269–286; k) S. Rej, Y. Ano, N. Chatani, *Chem. Rev.* **2020**, *120*, 1788–1887; l) H.-Y. Huang, A. Benzai, X. Shi, H. Doucet, *Chem. Rec.* **2021**, *21*, 343–356.
- [7] W. Hagui, H. Doucet, J.-F. Soule, *Chem* **2019**, *5*, 2006–2078.
- [8] Y. Aoyagi, A. Inoue, I. Koizumi, R. Hashimoto, A. Miyafuji, J. Kunoh, R. Honma, Y. Akita, A. Ohta, *Heterocycles* **1992**, *33*, 257–272.
- [9] For selected examples of intermolecular Pd-catalyzed direct C2-arylations of imidazoles: a) V. Gracias, A. F. Gasielki, T. G. Pagano, S. W. Djuric, *Tetrahedron Lett.* **2006**, *47*, 8873–8876; b) F. Bellina, S. Cauteruccio, R. Rossi, *Eur. J. Org. Chem.* **2006**, 1379–1382; c) I. Cerna, R. Pohl, B. Klepetarova, M. Hocek, *Org. Lett.* **2006**, *8*, 5389–5392; d) F. Bellina, C. Calandri, S. Cauteruccio, R. Rossi, *Tetrahedron* **2007**, *63*, 1970–1980; e) F. Bellina, S. Cauteruccio, R. Rossi, *J. Org. Chem.* **2007**, *72*, 8543–8546; f) T. E. Storr, A. G. Firth, K. Wilson, K. Darley, C. G. Baumann, I. J. S. Fairlamb, *Tetrahedron* **2008**, *64*, 6125–6137; g) D. Zhao, W. Wang, S. Lian, F. Yang, J. Lan, J. You, *Chem. Eur. J.* **2009**, *15*, 1337–1340; h) S. Fripiat, A. Peresson, T. Perse, Y. Ramondenc, C. Schneider, O. Querolle, P. Angibaud, V. Poncelet, L. Meerpoel, V. Levacher, L. Bischoff, C. Baudequin, C. Hoarau, *Synlett* **2020**, *31*, 1015–1021.
- [10] For selected examples of intermolecular Pd-catalyzed direct C5-arylations of imidazoles: a) Y. Kondo, T. Komine, T. Sakamoto, *Org. Lett.* **2000**, *2*, 3111–3113; b) F. Bellina, S. Cauteruccio, L. Mannina, R. Rossi, S. Viel, *J. Org. Chem.* **2005**, *70*, 3997–4005; c) B. B. Toure, B. S. Lane, D. Sames, *Org. Lett.* **2006**, *8*, 1979–1982; d) H. A. Chiong, O. Daugulis, *Org. Lett.* **2007**, *9*, 1449–1451; e) B. Liégaut, D. Lapointe, L. Caron, A. Vlassova, K. Fagnou, *J. Org. Chem.* **2009**, *74*, 1826–1834; f) F. Shibahara, E. Yamaguchi, T. Murai, *J. Org. Chem.*, **2011**, *76*, 2680–2693; g) F. Shibahara, T. Yamauchi, E. Yamaguchi, T. Murai, *J. Org. Chem.*, **2012**, *77*, 8815–8820; h) F. Bellina, M. Lessi, C. Manzini *Eur. J. Org. Chem.* **2013**, 5621–5630; i) S. Mao, X. Shi, J.-F. Soule, H. Doucet, *Adv. Synth. Catal.* **2018**, *360*, 3306–3317; j) J.-Y. Lee, D. Ghosh, Y.-T. Kuo, H. M. Lee, *Adv. Synth. Catal.* **2020**, *362*, 648–658.
- [11] For selected examples of intramolecular C-H arylations: a) L. C. Campeau, M. Parisien, A. Jean, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 581–590; b) D. Garcia-Cuadrado, A. A. C. Braga, F. Maseras, A. M. Echavarren, *J. Am. Chem. Soc.* **2006**, *128*, 1066–1067; c) L.-C. Campeau, K. Fagnou, *Chem. Commun.* **2006**, 1253–1264; d) J. Peng, T. Chen, C. Chen, B. Li, *J. Org. Chem.* **2011**, *76*, 9507–9513.
- [12] a) W. Hagui, K. Yuan, N. Besbes, E. Srasra, J.-F. Soule, H. Doucet, *ChemCatChem* **2015**, *7*, 3544–3554; b) J. Zhang, X. Shi, H. Doucet, *Eur. J. Org. Chem.* **2021**, 4974–4983.
- [13] J. Roger, H. Doucet, *Tetrahedron*, **2009**, *65*, 9772–9781.
- [14] T. Cantat, E. Génin, C. Giroud, G. Meyer, A. Jutand, *J. Organomet. Chem.* **2003**, *687*, 365–376.
- [15] For concerted metalation deprotonation mechanism: a) D. L. Davies, S. M. A. Donald, S. A. Macgregor, *J. Am. Chem. Soc.* **2005**, *127*, 13754–13755; b) M. Lafrance, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 16496–16497; c) S. I. Gorelsky, D. Lapointe, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 10848–10849; d) S. I. Gorelsky, *Coord. Chem. Rev.* **2013**, *257*, 153–164; e) D. L. Davies, S. A. Macgregor, C. L. McMullin, *Chem. Rev.* **2017**, *117*, 8649–8709; f) R. A. Alharis, C. L. McMullin, D. L. Davies, K. Singh, S. A. Macgregor, *J. Am. Chem. Soc.* **2019**, *141*, 8896–8906.
- [16] L.-C. Campeau, M. Parisien, A. Jean, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 581–590.

Entry for the Table of Contents

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From commercially available compounds using an air-stable Pd-catalyst precursor and KOPiv as inexpensive base, a wide variety of imidazo[1,5-f]phenanthridines was prepared. This one pot synthetic scheme allowed the first synthesis of imidazo[1,2-f]phenanthridine. Moreover, it permits the introduction of desired functional groups at positions 5, 7, 10 and 11 of imidazo[1,2-f]phenanthridines.