JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Phosphine-Free Palladium-Catalyzed Direct Arylation of Imidazo[1,2-a]pyridines with Aryl Bromides at Low Catalyst Loading

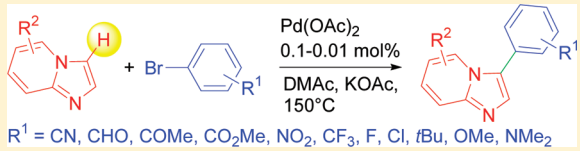
Hai Yan Fu,[†] Lu Chen,[‡] and Henri Doucet*[,‡]

[†]Key Laboratory of Green Chemistry and Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu, 610064, China

[‡]Institut Sciences Chimiques de Rennes, UMR 6226 CNRS-Université de Rennes "Catalyse et Organometalliques", Campus de Beaulieu, 35042 Rennes, France

Supporting Information

ABSTRACT: Ligand-free $Pd(OAc)_2$ was found to catalyze very efficiently the direct arylation of imidazo[1,2-a]pyridines at C3 under very low catalyst concentration. The reaction can be performed employing as little as 0.1−0.01 mol % catalyst with electron-deficient and some electron-excessive aryl bromides.



The palladium-catalyzed direct arylation of several heteroaromatics via a C−H bond activation using aryl halides has led to successes in recent years.[1−3] Such couplings are very attractive compared to classical palladium-catalyzed reactions such as Stille, Suzuki, or Negishi couplings,[4] as they do not require the preliminary synthesis of organometallic derivatives. However, the major drawback of most of the reported procedures is that they require 1−10 mol % palladium catalyst associated with 1−20 mol % of phosphine ligands. Only a few examples of such reactions using low catalyst loadings have been reported to date.[5] Among heterocycles, imidazo[1,2-a]pyridines display important biological properties. For example, Zolpidem is actually employed for the short-term treatment of insomnia, and Miroprofen is a nonsteroidal anti-inflammatory drug.

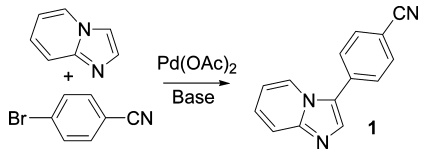
So far, the direct arylation of imidazo[1,2-a]pyridines generally requires quite high catalyst loadings (2−10 mol %).[6] For example, in 2006, Berteina-Raboin and co-workers reported that the use of 5 mol % $Pd(OAc)_2$ associated to 10 mol % PPh_3 promotes efficiently the coupling of imidazo[1,2-*a*]pyridines with aryl bromides at the 3-position.[6a] The same year, Sames and co-workers employed 2.5 mol % of a palladium complex containing an imidazolyl carbene and PPh_3 as ligands for the coupling of methyl 4-bromobenzoate with ethyl imidazo[1,2-a]pyridine-2-carboxylate. The C3 arylated imidazo-[1,2-a]pyridine was obtained in 51% yield.[6b] Therefore, the discovery of more effective conditions for the direct coupling of imidazo[1,2-a]pyridine derivatives with aryl bromides, especially under low catalyst loading conditions, would be a considerable advantage for industrial applications.

In 2003, de Vries and co-workers described extremely promising results for the Heck and Suzuki reactions using a low loading (0.1−0.01 mol %) of ligand-free catalyst $Pd(OAc)_2$.[7,8] They demonstrated that, at elevated temperature, when $Pd(OAc)_2$ is employed as the catalyst precursor, soluble palladium(0) colloids or nanoparticles are formed and that the Heck or Suzuki reaction takes place. We have recently reported that the use of the "de Vries conditions" allows the coupling of several heteroaromatics using ligand-free palladium catalyst.[5b−d] However, so far, such procedure has not been employed for the direct arylation of imidazo[1,2-a]pyridines. Here, we wish to report on the reaction of imidazo[1,2-a]pyridines using a wide variety of electronically and sterically diverse aryl or heteroaryl bromides using low loadings of a phosphine-free palladium catalyst.

We decided to employ commercially available imidazo[1,2-a]pyridine and 4-bromobenzonitrile as the test substrates for our study (Scheme 1, Table 1). We initially examined the influence of the nature of the base on the conversion for this reaction using DMAc as the solvent and 0.1 mol % $Pd(OAc)_2$ as the catalyst. In the presence of KOAc as the base, a complete conversion of 4-bromobenzonitrile was observed, and **1** was obtained in 93% yield (Table 1, entry 1). A similar result was obtained in the presence of CsOAc as the base, whereas NaOAc led only to a conversion of 88% of 4-bromobenzonitrile (Table 1, entries 2 and 3). On the other hand, K_2CO_3 or Cs_2CO_3 gave moderate conversions of 4-bromobenzonitrile (Table 1, entries 4 and 5). The good performance of acetates as the base is consistent with a concerted metalation deprotonation (CMD) pathway.[9] The nature of the solvent often modifies the catalyst activity in cross-coupling reactions; thus, we observed that NMP and DMF in the presence of 0.1 mol % $Pd(OAc)_2$ as the catalyst also gave **1** in high yields with complete conversion of 4-bromobenzonitrile (Table 1, entries 6 and 7). Some solvents that can be considered as "greener" than DMAc, NMP or DMF, have also been employed. Pentan-1-ol[10a] and cyclopentyl methyl ether[10b] led to complete conversions of 4-bromobenzonitrile and to good yields in **1** (Table 1, entries 10 and 11). Diethylcarbonate[10c] was also found to quite efficiently promote the reaction (Table 1, entry 9). On the other hand, the reaction performed in absence of solvent led to a poor conversion of the aryl bromide (Table 1,

Received: March 12, 2012
Published: April 16, 2012

Table 1. Influence of the Reaction Conditions on the Arylation of Imidazo[1,2-a]pyridine with 4-Bromobenzonitrile[a]



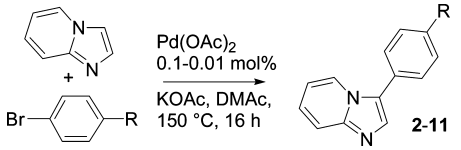
entry	solvent	base	$Pd(OAc)_2$ (mol %)	convn. (%)
1	DMAc	KOAc	0.1	100 (93)
2	DMAc	CsOAc	0.1	98
3	DMAc	NaOAc	0.1	88
4	DMAc	K_2CO_3	0.1	66
5	DMAc	Cs_2CO_3	0.1	45
6	NMP	KOAc	0.1	100
7	DMF	KOAc	0.1	100
8	xylene	KOAc	0.1	75
9	diethylcarbonate	KOAc	0.1	82[b]
10	pentan-1-ol	KOAc	0.1	100 (87)
11	cyclopentyl methyl ether	KOAc	0.1	99[c]
12	No solvent	KOAc	0.1	38
13	DMAc	KOAc	0.01	86 (80)
14	NMP	KOAc	0.01	85
15	DMF	KOAc	0.01	0
16	diethylcarbonate	KOAc	0.01	0[b]
17	pentan-1-ol	KOAc	0.01	55
18	cyclopentyl methyl ether	KOAc	0.01	23
19	DMAc	KOAc	0.1	86[d]
20	DMAc	KOAc	0.1	93 (83)[e]
21	DMAc	KOAc	0.1	92 (87)[f]
22	DMAc	KOAc	1	100 (91)[f]
23	DMAc	KOAc	2	93 (87)[g]
24	DMAc	KOAc	0.01	84 (77)[h]

[a]Conditions: $Pd(OAc)_2$, 4-bromobenzonitrile (1 equiv), imidazo[1,2-a]pyridine (1.5 equiv), base (2 equiv), 16 h, 150 °C, conversion of 4-bromobenzonitrile; isolated yields of **1** are given in parentheses. [b]130 °C. [c]125 °C. [d]100 °C. [e]Imidazo[1,2-a]pyridine (1.1 equiv). [f]1 h. [g]0.25 h. [h]4-Bromobenzonitrile (30 mmol), imidazo[1,2-a]pyridine (45 mmol), KOAc (60 mmol), DMAc (45 mL), 16 h, 150 °C.

entry 12). Then, we performed the reactions using only 0.01 mol % catalyst with these solvents (Table 1, entries 13−17). Only DMAc and NMP gave good conversions of 4-bromobenzonitrile. It sould be noted that the reaction can be performed using only a slight excess of imidazo[1,2-a]pyridine (1.1 equiv) (Table 1, entry 20) or shorter reaction times. For example, in the presence of 0.1 or 1 mol % catalyst, conversions of 92% and 100% were obtained after only 1 h (Table 1, entries 21 and 22). In the presence of 2 mol % $Pd(OAc)_2$, a conversion of 93% of 4-bromobenzonitrile was obtained after 15 min (Table 1, entry 23). A scale up experiment was also successful, as reactions performed on 1 or 30 mmol scale led to very similar yields (Table 1, entries 13 and 24).

Then, imidazo[1,2-a]pyridine was coupled with several other aryl bromides in the presence of 0.1−0.01 mol % $Pd(OAc)_2$, KOAc as the base in DMAc, pentan-1-ol, or diethylcarbonate (Tables 2 and 3, Schemes 1−3). Selective 3-arylations were observed using the *para*-substituted electron-deficient aryl bromides, 4-bromoacetophenone, 4-bromobenzaldehyde, methyl 4-bromobenzoate, 4-bromonitrobenzene, or 4-trifluoromethylbromobenzene, resulting in 72−93% yields of the products **2**−**6** (Table 2, entries 1−3, 6−8, and 10). In all cases, the expected 3-arylated imidazo[1,2-a]pyridines were selectively obtained. Again, good yields in **3** or **5** could be obtained using diethylcarbonate or pentan-1-ol as the solvents (Table 2, entries 4, 5, and 9). 4-Fluorobromobenzene was also successfully coupled with imidazo[1,2-a]pyridine to give **7** in 80% yield (Table 2, entry 11). It should be noted that even 4-chlorobromobenzene could be employed to give **8** in 82% yield (Table 2, entry 12). In the course of this reaction, no cleavage of the C−Cl bond was observed, allowing further transformations. Even the use of electron-rich aryl bromide, 4-*tert*-butylbromobenzene, led to **9** in a good yield of 78%, when 0.1 mol % catalyst was employed (Table 2, entry 14). On the other hand, under these conditions, a partial conversion of 4-bromoanisole or 4-bromo-*N*,*N*-dimethylaniline was observed, and **10** and **11** were obtained in slightly lower yields of 65% and 63% (Table 2, entries 15 and 16).

Table 2. Direct Arylation of Imidazo[1,2-a]pyridine with *para*-Substituted Aryl Bromides[a]



entry	R	ratio substrate/catalyst	product	yield (%)
1	COMe	1000	**2**	92
2	COMe	10000	**2**	74
3	CHO	10000	**3**	80
4	CHO	1000	**3**	79[b]
5	CHO	1000	**3**	78[c]
6	CO_2Me	1000	**4**	93
7	CO_2Me	10000	**4**	87
8	NO_2	10000	**5**	88
9	NO_2	1000	**5**	89[b]
10	CF_3	1000	**6**	72
11	F	1000	**7**	80
12	Cl	1000	**8**	82
13	Cl	1000	**8**	40[c]
14	*t*-Bu	1000	**9**	78
15	MeO	1000	**10**	65
16	NMe_2	1000	**11**	63

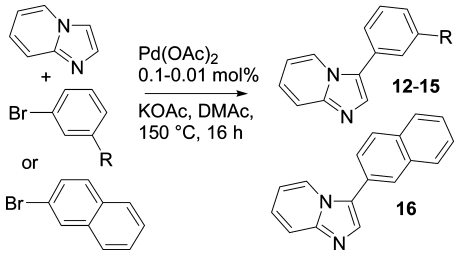
[a]Conditions: $Pd(OAc)_2$ (0.001 or 0.0001 equiv), aryl bromide (1 equiv), imidazo[1,2-a]pyridine (1.5 equiv), KOAc (2 equiv), 16 h, 150 °C. [b]Pentan-1-ol as the solvent. [c]Diethylcarbonate as the solvent, 130 °C.

The *meta*-substituted aryl bromides, 3-bromobenzonitrile, 3-bromobenzaldehyde, or 3-trifluoromethylbromobenzene, gave **12**−**14** in 71−93% yields using 0.1−0.01 mol % $Pd(OAc)_2$ (Table 3, entries 1−5). A lower yield of 53% in **15** was obtained in the presence of 3-chlorobromobenzene because of a partial conversion of this aryl bromide (Table 3, entry 7). 2-Bromonaphthalene was also found to be suitable coupling partner and gave **16** in 82% in the presence of only 0.01 mol % catalyst (Table 3, entry 9).

Then, we employed a range of *ortho*-substituted aryl bromides (Scheme 1). Similar yields were obtained with 2-bromobenzonitrile and 2-trifluoromethylbromobenzene than with the *para*-substituted aryl bromides. From these two reactants, **17** and **18** were obtained in 92 and 70% yields, resprectively. On the other hand, ethyl 2-bromobenzoate led to

dx.doi.org/10.1021/jo300528b | J. Org. Chem. 2012, 77, 4473−4478

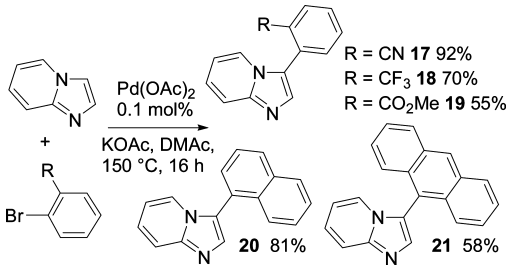
Table 3. Direct Arylation of Imidazo[1,2-a]pyridine with *meta*-Substituted Aryl Bromides[a]



entry	R or ArBr	ratio substrate/catalyst	prod.	yield (%)
1	CN	1000	**12**	93
2	CN	10000	**12**	90
3	CHO	1000	**13**	71
4	CHO	1000	**13**	20[b]
5	CF_3	1000	**14**	83
6	CF_3	10000	**14**	32
7	Cl	1000	**15**	53
8	2-bromonaphthalene	1000	**16**	88
9	2-bromonaphthalene	10000	**16**	82

[a]Conditions: $Pd(OAc)_2$ (0.001 or 0.0001 equiv), aryl bromide (1 equiv), imidazo[1,2-a]pyridine (1.5 equiv), KOAc (2 equiv), 16 h, 150 °C. [b]Diethylcarbonate as the solvent, 130 °C.

Scheme 1. Direct Arylation of Imidazo[1,2-a]pyridine with *ortho*-Substituted Aryl Bromides



19 in only 55% yield. A high reactivity of 1-bromonaphthalene was also observed to produce **20** in 81% yield. Finally, the more congested aryl bromide, 9-bromoanthracene, was employed. The target product **21** was isolated in 58% yield. In the course of this reaction, the formation of anthracene from dehalogenation of 9-bromoanthracene was also observed in 10% yield. It should be noted that these five reactions were performed using only 0.1 mol % $Pd(OAc)_2$ as the catalyst.

Some imidazo[1,2-a]pyridines substituted at C3 by pyrimidines have been found to be efficient as cyclin-dependent kinase inhibitors.[11] We observed that such heteroaryl bromides are also suitable reactants. The coupling of 3- or 4-bromopyridines, 3-bromoquinoline, 4-bromoisoquinoline, or 5-bromopyrimidine, with imidazo[1,2-a]pyridine in the presence of 0.1 mol % $Pd(OAc)_2$ proceed nicely to give **22**−**26** in 73−92% yields (Scheme 2).

The poly-heteroarylation of polybromobenzene would give a simple access to conjugated compounds. Again, using only 0.1 mol % $Pd(OAc)_2$ as the catalyst, 2,7-dibromofluorene or 1,4-dibromonaphthalene were diheteroarylated with imidazo[1,2-a]pyridine to give **27** and **28** in very high yields (Scheme 3, top). In the presence of 9,10-dibromoanthracene, the desired coupling product **29** was obtained in a lower yield of 59% because of the formation of a small amount of **21** as side-product. 1,3,5-Tribromobenzene was also successfully employed to prepare the 1,3,5-tri(heteroaryl)benzene **30** in 84% yield (Scheme 3, bottom). Surprisingly, no mono- or di-heteroarylated benzene derivatives were isolated in the course of this reaction.

The reaction is not limited to the use of imidazo[1,2-a]pyridine. Under the same reaction conditions, imidazo[1,2-a]pyridine-6-carbonitrile was successfully coupled with 4-bromobenzaldehyde or 2-bromonaphthalene to give **31** and **32** in 64 and 72% yields, respectively (Scheme 4).

In summary, we have demonstrated that using as little as 0.1−0.01 mol % of $Pd(OAc)_2$ as catalyst precursor, the direct 3-arylation via C−H bond activation of imidazo[1,2-a]pyridines proceeds in moderate to very high yields. We also observed that some solvents considered as "greener" than DMAc can be employed.

EXPERIMENTAL SECTION

General Procedure. As a typical experiment, the reaction of the aryl bromide (1 mmol), imidazo[1,2-a]pyridine (0.177 g, 1.5 mmol) or imidazo[1,2-a]pyridine-6-carbonitrile (0.186 g, 1.3 mmol), and KOAc (0.196 g, 2 mmol) at 150 °C during 16 h in DMAc (4 mL) in the presence of $Pd(OAc)_2$ (0.224 mg, 0.001 mmol or 0.0224 mg, 0.0001 mmol; see tables or schemes), under argon affords the coupling product after evaporation of the solvent and purification on silica gel.

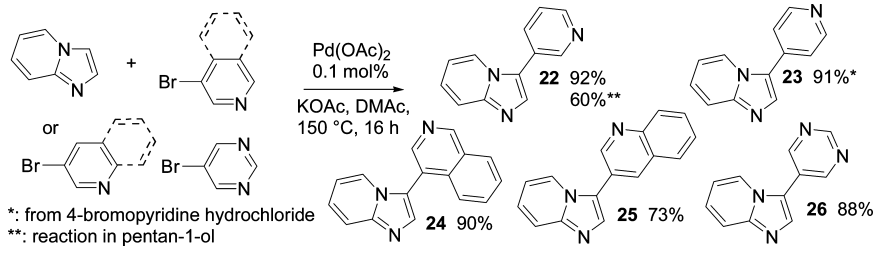
4-Imidazo[1,2-a]pyridin-3-ylbenzonitrile (1). 4-Bromobenzonitrile (0.182 g, 1 mmol) affords **1** in 80% (0.175 g) yield; light amorphous yellow solid; mp 175−176 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, J = 6.9 Hz, 1H), 7.73 (s, 1H), 7.72 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.2 Hz, 3H), 7.21 (t, J = 7.2 Hz, 1H), 6.85 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.8, 134.0, 133.7, 132.8, 127.4, 125.0, 123.7, 123.0, 118.4, 113.2, 110.9. Elemental analysis calcd (%) for $C_{14}H_9N_3$ (219.24): C 76.70, H 4.14. Found: C 76.81, H 4.10.

4-Imidazo[1,2-a]pyridin-3-ylacetophenone (2). 4-Bromoacetophenone (0.199 g, 1 mmol) affords **2** in 92% (0.217 g) yield; amorphous white solid; mp 161−162 °C.

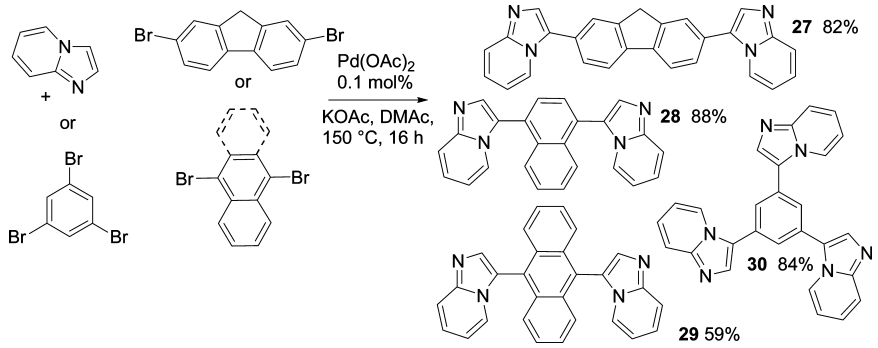
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, J = 6.9 Hz, 1H), 8.06 (d, J = 8.2 Hz, 2H), 7.75 (s, 1H), 7.70−7.60 (m, 3H), 7.21 (t, J = 7.2 Hz, 1H), 6.84 (t, J = 7.2 Hz, 1H). 2.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.0, 146.7, 136.0, 133.8, 133.6, 129.2, 127.1, 124.7, 124.6,

Scheme 2. Direct Arylation of Imidazo[1,2-a]pyridine with Heteroaryl Bromides

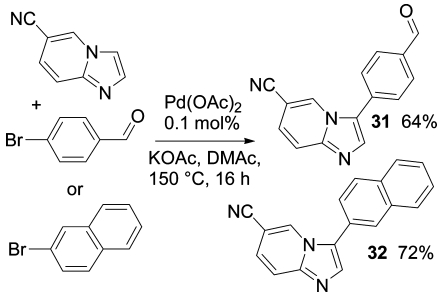


dx.doi.org/10.1021/jo300528b | J. Org. Chem. 2012, 77, 4473−4478

Scheme 3. Direct Arylation of Imidazo[1,2-a]pyridine with Di- or Tribromobenzene Derivatives or a Dibromofluorene



Scheme 4. Direct Arylation of Imidazo[1,2-a]pyridine-6-carbonitrile with Aryl Bromides



123.2, 118.3, 113.0, 26.5. Elemental analysis calcd (%) for $C_{15}H_{12}N_2O$ (236.27): C 76.25, H 5.12. Found: C 76.21, H 5.04.

4-Imidazo[1,2-a]pyridin-3-ylbenzaldehyde (3). 4-Bromobenzaldehyde (0.185 g, 1 mmol) affords **3** in 80% (0.178 g) yield; amorphous light yellow solid; mp 110−111 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.96 (s, 1H), 8.35 (d, J = 6.9 Hz, 1H), 7.92 (d, J = 8.2 Hz, 2H), 7.74 (s, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 8.2 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 6.81 (t, J = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.1, 146.8, 135.1, 135.0, 133.9, 130.4, 127.2, 124.9, 124.3, 123.2, 118.3, 113.1. Elemental analysis calcd (%) for $C_{14}H_{10}N_2O$ (222.24): C 75.66, H 4.54. Found: C 75.50, H 4.62.

Methyl 4-Imidazo[1,2-a]pyridin-3-ylbenzoate (4). Methyl 4-bromobenzoate (0.215 g, 1 mmol) affords **4** in 93% (0.235 g) yield; amorphous white solid; mp 147−149 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (d, J = 6.9 Hz, 1H), 8.18 (d, J = 8.2 Hz, 2H), 7.79 (s, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 6.89 (t, J = 7.2 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 146.8, 133.8, 133.6, 130.5, 129.4, 127.2, 124.8, 123.4, 118.5, 113.0, 52.3. Elemental analysis calcd (%) for $C_{15}H_{12}N_2O_2$ (252.27): C 71.42, H 4.79. Found: C 71.30, H 4.64.

3-(4-Nitrophenyl)-imidazo[1,2-a]pyridine (5).[12] 4-Bromonitrobenzene (0.202 g, 1 mmol) affords **5** in 88% (0.210 g) yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (d, J = 6.8 Hz, 1H), 8.31 (d, J = 8.0 Hz, 2H), 7.78 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 6.88 (t, J = 6.4 Hz, 1H).

3-(4-Trifluoromethylphenyl)-imidazo[1,2-a]pyridine (6). 4-Trifluoromethylbromobenzene (0.225 g, 1 mmol) affords **6** in 72% (0.189 g) yield; amorphous white yellow solid; mp 150−151 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (d, J = 6.9 Hz, 1H), 7.77−7.56 (m, 6H), 7.22 (t, J = 7.2 Hz, 1H), 6.83 (t, J = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.6, 133.5, 132.9, 129.8 (q, J = 32.9 Hz), 127.7, 126.1 (q, J = 3.9 Hz), 124.7, 124.2, 123.9 (q, J = 272.3 Hz), 123.1, 118.4, 113.0. Elemental analysis calcd (%) for $C_{14}H_9F_3N_2$ (262.23): C 64.12, H 3.46. Found: C 64.24, H 3.35.

3-(4-Fluorophenyl)-imidazo[1,2-a]pyridine (7).[13] 4-Bromofluorobenzene (0.175 g, 1 mmol) affords 7 in 80% (0.170 g) yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 6.2 Hz, 1H), 7.62 (m, 2H), 7.47−7.44 (m, 2H), 7.17−7.12 (m, 3H), 6.75 (t, J = 6.7 Hz, 1H).

3-(4-Chlorophenyl)-imidazo[1,2-a]pyridine (8).[6c] 4-Bromochlorobenzene (0.191 g, 1 mmol) affords **8** in 82% (0.187 g) yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (m, 1H), 7.62 (m, 2H), 7.41 (m, 4H), 7.14 (m, 1H), 6.75 (m, 1H).

3-(4-*t*-Butylphenyl)-imidazo[1,2-a]pyridine (9). 4-*tert*-Butylbromobenzene (0.213 g, 1 mmol) affords **9** in 78% (0.195 g) yield; amorphous white solid; mp 143−145 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 6.9 Hz, 1H), 7.67 (s, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 6.77 (t, J = 6.8 Hz, 1H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.2, 145.9, 132.2, 127.7, 126.3, 126.1, 125.6, 123.9, 123.4, 118.1, 112.3, 34.7, 31.2. Elemental analysis calcd (%) for $C_{17}H_{18}N_2$ (250.34): C 81.56, H 7.25. Found: C 81.69, H 7.36.

3-(4-Methoxyphenyl)-imidazo[1,2-a]pyridine (10).[13] 4-Bromoanisole (0.187 g, 1 mmol) affords **10** in 65% (0.146 g) yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J = 6.8 Hz, 1H), 7.62−7.59 (m, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.12 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 2H), 6.73 (t, J = 6.8 Hz, 1H), 3.83 (s, 6H).

(4-Imidazo[1,2-a]pyridin-3-yl-phenyl)-dimethylamine (11). 4-Bromo-*N*,*N*-dimethylaniline (0.200 g, 1 mmol) affords **11** in 63% (0.149 g) yield; amorphous yellow solid; mp 137−139 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J = 6.9 Hz, 1H), 7.52−7.48 (m, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.02 (t, J = 7.2 Hz, 1H), 6.72 (d, J = 8.2 Hz, 2H), 6.63 (t, J = 7.2 Hz, 1H), 2.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 145.4, 131.3, 129.1, 126.0, 123.4, 123.3, 117.8, 116.4, 112.5, 111.9, 40.2. Elemental analysis calcd (%) for $C_{15}H_{15}N_3$ (237.30): C 75.92, H 6.37. Found: C 75.68, H 6.30.

3-Imidazo[1,2-a]pyridin-3-ylbenzonitrile (12). 3-Bromobenzonitrile (0.182 g, 1 mmol) affords **12** in 93% (0.204 g) yield; amorphous white solid; mp 138−140 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J = 6.9 Hz, 1H), 7.73 (s, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.63 (s, 1H), 7.60−7.49 (m, 3H), 7.14 (t, J = 7.2 Hz, 1H), 6.78 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 133.2, 131.5, 130.9, 130.5, 130.5, 129.9, 124.7, 123.0, 122.6, 118.1, 117.9, 113.2, 112.9. Elemental analysis calcd (%) for $C_{14}H_9N_3$ (219.24): C 76.70, H 4.14. Found: C 76.68, H 4.07.

3-Imidazo[1,2-a]pyridin-3-ylbenzaldehyde (13). 3-Bromobenzaldehyde (0.185 g, 1 mmol) affords **13** in 71% (0.158 g) yield; amorphous gray solid; mp 41−42 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.09 (s, 1H), 8.32 (d, J = 6.9 Hz, 1H), 8.07 (s, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.77 (s, 1H), 7.75−7.63 (m, 2H), 7.24 (t, J = 7.2 Hz, 1H), 6.86 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 146.4, 137.2, 133.6, 133.0, 130.4, 130.1, 129.5, 128.3, 124.9, 124.3, 123.1, 118.4, 113.2. Elemental analysis calcd (%) for $C_{14}H_{10}N_2O$ (222.24): C 75.66, H 4.54. Found: C 75.57, H 4.50.

3-(3-Trifluoromethylphenyl)-imidazo[1,2-a]pyridine (14). 3-Trifluoromethylbromobenzene (0.225 g, 1 mmol) affords **14** in 83% (0.218 g) yield; amorphous white solid; mp 79−80 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 7.9 Hz, 1H), 7.79 (s, 1H), 7.75−7.60 (m, 5H), 7.20 (t, J = 7.2 Hz, 1H), 6.83 (t, J = 7.2 Hz,

dx.doi.org/10.1021/jo300528b | J. Org. Chem. 2012, 77, 4473−4478

1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 133.3, 131.7 (q, J = 32.4 Hz), 131.0, 130.2, 129.8, 124.7 (q, J = 3.9 Hz), 124.6, 124.4 (q, J = 3.9 Hz), 124.2, 123.9 (q, J = 272.8 Hz), 123.0, 118.5, 113.1. Elemental analysis calcd (%) for $C_{14}H_9F_3N_2$ (262.23): C 64.12, H 3.46. Found: C 64.02, H 3.54.

3-(3-Chlorophenyl)-imidazo[1,2-a]pyridine (15). 3-Bromochlorobenzene (0.191 g, 1 mmol) affords **15** in 53% (0.121 g) yield; clear oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, J = 6.9 Hz, 1H), 7.66 (s, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.49 (s, 1H), 7.42−7.28 (m, 3H), 7.16 (t, J = 7.0 Hz, 1H), 6.78 (t, J = 7.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.2, 135.0, 133.0, 130.9, 130.3, 128.0, 127.6, 125.7, 124.4, 124.1, 123.0, 118.2, 112.7. Elemental analysis calcd (%) for $C_{13}H_9ClN_2$ (228.68): C 68.28, H 3.97. Found: C 68.34, H 3.80.

3-Naphthalen-2-yl-imidazo[1,2-a]pyridine (16). 2-Bromonaphthalene (0.207 g, 1 mmol) affords **16** in 88% (0.215 g) yield; amorphous light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, J = 6.9 Hz, 1H), 7.96 (s, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.88−7.80 (m, 2H), 7.77 (s, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.55−7.45 (m, 2H), 7.17 (t, J = 8.0 Hz, 1H), 6.77 (t, J = 6.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 133.4, 132.7, 132.6, 128.8, 127.8, 127.6, 126.6, 126.5, 126.4, 126.3, 125.5, 124.2, 123.2, 118.1, 112.5. Elemental analysis calcd (%) for $C_{17}H_{12}N_2$ (244.29): C 83.58, H 4.95. Found: C 83.70, H 4.99.

2-Imidazo[1,2-a]pyridin-3-ylbenzonitrile (17). 2-Bromobenzonitrile (0.182 g, 1 mmol) affords **17** in 92% (0.202 g) yield; amorphous white solid; 146−147 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 6.9 Hz, 1H), 7.86 (s, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.75−7.63 (m, 2H), 7.59 (d, J = 8.2 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 6.82 (t, J = 6.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 134.7, 134.1, 133.1, 132.4, 129.8, 128.6, 125.1, 123.3, 121.2, 118.2, 117.6, 112.9, 112.3. Elemental analysis calcd (%) for $C_{14}H_9N_3$ (219.24): C 76.70, H 4.14. Found: C 76.89, H 4.21.

3-(2-Trifluoromethylphenyl)-imidazo[1,2-a]pyridine (18). 2-Trifluoromethylbromobenzene (0.225 g, 1 mmol) affords **18** in 70% (0.184 g) yield; amorphous white solid; mp 103−104 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, J = 7.6 Hz, 1H), 7.75−7.55 (m, 5H), 7.46 (d, J = 7.2 Hz, 1H), 7.18 (t, J = 7.8 Hz, 1H), 6.73 (t, J = 6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6, 133.9, 133.1, 132.0, 131.1 (q, J = 30.2 Hz), 129.4, 127.5, 126.8 (q, J = 5.0 Hz), 124.3, 123.5, 123.1 (q, J = 273.5 Hz), 121.7, 117.8, 112.4. Elemental analysis calcd (%) for $C_{14}H_9F_3N_2$ (262.23): C 64.12, H 3.46. Found: C 64.05, H 3.56.

Methyl 2-imidazo[1,2-a]pyridin-3-yl-benzoate (19). Methyl 2-bromobenzoate (0.215 g, 1 mmol) affords **19** in 55% (0.139 g) yield; amorphous light yellow solid; 72−74 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 7.5 Hz, 1H), 7.73 (d, J = 6.0 Hz, 1H), 7.65−7.43 (m, 4H), 7.48 (d, J = 7.2 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 6.73 (t, J = 6.6 Hz, 1H), 3.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 145.7, 132.8, 132.6, 132.5, 131.1, 131.0, 129.2, 129.0, 124.6, 124.1, 123.7, 117.9, 112.0, 52.2. Elemental analysis calcd (%) for $C_{15}H_{12}N_2O_2$ (252.27): C 71.42, H 4.79. Found: C 71.51, H 4.89.

3-Naphthalen-1-ylimidazo[1,2-a]pyridine (20).[13] 1-Bromonaphthalene (0.207 g, 1 mmol) affords **20** in 81% (0.198 g) yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (m, 2H), 7.77 (s, 1H), 7.72 (d, J = 10.8 Hz, 1H), 7.66 (d, J = 6.8 Hz, 1H), 7.56 (s, 2H), 7.49 (m, 2H), 7.37 (m, 1H), 7.17 (t, J = 7.5 Hz, 1H), 6.64 (t, J = 6.6 Hz, 1H).

3-Anthracen-9-ylimidazo[1,2-a]pyridine (21). 9-Bromoanthracene (0.257 g, 1 mmol) affords **21** in 58% (0.171 g) yield; amorphous white solid; mp 208−209 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.83 (s, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.45 (d, J = 8.4 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.29 (t, J = 7.5 Hz, 2H), 7.22 (d, J = 6.8 Hz, 1H), 7.17 (t, J = 6.4 Hz, 1H), 6.54 (t, J = 6.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 135.5, 131.8, 131.5, 129.1, 128.8, 126.7, 125.6, 125.5, 124.3, 124.1, 122.0, 120.6, 118.0, 112.3. Elemental analysis calcd (%) for $C_{21}H_{14}N_2$ (294.35): C 85.69, H 4.79. Found: C 85.80, H 4.65.

3-Pyridin-3-ylimidazo[1,2-a]pyridine (22). 3-Bromopyridine (0.158 g, 1 mmol) affords **22** in 92% (0.179 g) yield; amorphous gray solid; mp 38−39 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (s, 1H), 8.65 (d, J = 3.5 Hz, 1H), 8.27 (d, J = 6.7 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.75 (s, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.45 (t, J = 7.0 Hz, 1H), 7.24 (t, J = 7.2 Hz, 1H), 6.86 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 148.8, 146.6, 135.1, 133.3, 125.6, 124.8, 123.9, 122.9, 122.3, 118.5, 113.1. Elemental analysis calcd (%) for $C_{12}H_9N_3$ (195.22): C 73.83, H 4.65. Found: C 73.94, H 4.51.

3-Pyridin-4-ylimidazo[1,2-a]pyridine (23). 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) affords **23** in 91% (0.177 g) yield; amorphous light yellow solid; mp 126−128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 8.1 Hz, 1H), 8.06 (d, J = 6.8 Hz, 2H), 7.76 (s, 1H), 7.68−7.62 (m, 3H), 7.21 (t, J = 7.2 Hz, 1H), 6.84 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.6, 147.2, 136.8, 134.4, 125.2, 123.4, 123.0, 120.9, 118.5, 113.3. Elemental analysis calcd (%) for $C_{12}H_9N_3$ (195.22): C 73.83, H 4.65. Found: C 73.74, H 4.50.

4-Imidazo[1,2-a]pyridin-3-ylisoquinoline (24). 4-Bromoisoquinoline (0.208 g, 1 mmol) affords **24** in 90% (0.221 g) yield; amorphous white solid; mp 168−169 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.65 (s, 1H), 8.12−8.07 (m, 1H), 7.84 (s, 1H), 7.79−7.60 (m, 4H), 7.57−7.50 (m, 1H), 7.25 (t, J = 7.8 Hz, 1H), 6.76 (t, J = 6.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 146.4, 144.6, 134.6, 134.4, 131.3, 128.4, 128.3, 127.8, 124.6, 124.1, 123.8, 120.3, 120.2, 118.2, 112.5. Elemental analysis calcd (%) for $C_{16}H_{11}N_3$ (245.28): C 78.35, H 4.52. Found: C 78.32, H 4.57.

3-Imidazo[1,2-a]pyridin-3-ylquinoline (25). 3-Bromoquinoline (0.208 g, 1 mmol) affords **25** in 73% (0.179 g) yield; amorphous white yellow solid; mp 146−148 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.09 (s, 1H), 8.34 (d, J = 6.9 Hz, 1H), 8.29 (s, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.83 (s, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.70 (d, J = 7.0 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.24 (t, J = 7.2 Hz, 1H), 6.86 (t, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 147.5, 146.7, 133.9, 133.7, 130.0, 129.5, 127.9, 127.8, 127.5, 124.9, 123.0, 122.7, 122.5, 118.6, 113.2. Elemental analysis calcd (%) for $C_{16}H_{11}N_3$ (245.28): C 78.35, H 4.52. Found: C 78.46, H 4.80.

3-Pyrimidin-5-ylimidazo[1,2-a]pyridine (26). 5-Bromopyrimidine (0.159 g, 1 mmol) affords **26** in 88% (0.172 g) yield; amorphous white solid; mp 196−197 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (s, 1H), 8.94 (s, 2H), 8.23 (d, J = 6.5 Hz, 1H), 7.78 (s, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.26 (t, J = 7.2 Hz, 1H), 6.89 (t, J = 6.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 155.2, 147.1, 134.1, 125.4, 124.3, 122.6, 118.7, 118.6, 113.6. Elemental analysis calcd (%) for $C_{11}H_8N_4$ (196.21): C 67.34, H 4.11. Found: C 67.51, H 4.04.

2,7-Bis(imidazo[1,2-a]pyridine)-fluorene (27). 2,7-Dibromofluorene (0.324 g, 1 mmol), imidazo[1,2-a]pyridine (0.354 g, 3 mmol), and KOAc (0.392 g, 4 mmol) at 150 °C during 16 h in DMAc (4 mL) in the presence of $Pd(OAc)_2$ (0.224 mg, 0.001 mmol) affords **27** in 82% (0.328 g) yield; amorphous orange solid, mp 229−231 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, J = 6.0 Hz, 2H), 7.94 (d, J = 7.2 Hz, 2H), 7.76 (s, 4H), 7.69 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.21 (t, J = 7.6 Hz, 2H), 6.83 (t, J = 6.2 Hz, 2H), 4.07 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.2, 144.3, 141.1, 132.6, 127.9, 126.8, 125.9, 124.6, 124.2, 123.4, 120.7, 118.3, 112.6, 37.0. Elemental analysis calcd (%) for $C_{27}H_{20}N_4$ (400.47): C 80.98, H 5.03. Found: C 80.99, H 5.14.

1,4-Bis(imidazo[1,2-a]pyridine)-naphthalene (28). 1,4-Dibromonaphthalene (0.286 g, 1 mmol), imidazo[1,2-a]pyridine (0.354 g, 3 mmol), and KOAc (0.392 g, 4 mmol) at 150 °C during 16 h in DMAc (4 mL) in the presence of $Pd(OAc)_2$ (0.224 mg, 0.001 mmol) affords **28** in 88% (0.317 g) yield; amorphous light yellow solid; mp 246−247 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (s, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.6 Hz, 2H), 7.69 (s, 2H), 7.66−7.60 (m, 2H), 7.47−7.41 (m, 2H), 7.21 (t, J = 7.2 Hz, 2H), 6.72 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9, 134.1, 132.4, 128.5, 127.8, 127.3,

dx.doi.org/10.1021/jo300528b | J. Org. Chem. 2012, 77, 4473−4478

125.9, 124.4, 123.9, 123.0, 118.0, 112.4. Elemental analysis calcd (%) for $C_{24}H_{16}N_4$ (360.41): C 79.98, H 4.47. Found: C 79.87, H 4.37.

9,10-Bis(imidazo[1,2-a]pyridine)-anthracene (29). 9,10-Dibromoanthracene (0.336 g, 1 mmol), imidazo[1,2-a]pyridine (0.354 g, 3 mmol), and KOAc (0.392 g, 4 mmol) at 150 °C during 16 h in DMAc (4 mL) in the presence of $Pd(OAc)_2$ (0.224 mg, 0.001 mmol) affords **29** in 59% (0.242 g) yield; amorphous yellow solid; mp 376−378 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (s, 2H), 7.85 (d, J = 9.0 Hz, 2H), 7.65−7.60 (m, 4H), 7.42−7.35 (m, 6H), 7.28 (t, J = 7.8 Hz, 2H), 6.70 (t, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1, 136.5, 131.8, 126.9, 126.2, 124.9, 124.7, 124.0, 120.3, 118.0, 112.7. Elemental analysis calcd (%) for $C_{28}H_{18}N_4$ (410.47): C 81.93, H 4.42. Found: C 81.80, H 4.54.

1,3,5-Tris(imidazo[1,2-a]pyridine)-benzene (30). 1,3,5-Tribromobenzene (0.315 g, 1 mmol), imidazo[1,2-a]pyridine (0.708 g, 6 mmol), and KOAc (0.588 g, 6 mmol) at 150 °C during 16 h in DMAc (4 mL) in the presence of $Pd(OAc)_2$ (0.224 mg, 0.001 mmol) affords affords **30** in 84% (0.358 g) yield; amorphous gray solid; mp 249−250 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, J = 5.9 Hz, 3H), 7.80 (s, 3H), 7.78 (s, 3H), 7.67 (d, J = 8.8 Hz, 3H), 7.21 (t, J = 7.2 Hz, 3H). 6.85 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 133.2, 131.7, 126.3, 124.7, 124.3, 123.1, 118.4, 113.1. Elemental analysis calcd (%) for $C_{27}H_{18}N_6$ (426.47): C 76.04, H 4.25. Found: C 76.10, H 4.21.

3-(4-Formylphenyl)-imidazo[1,2-a]pyridine-6-carbonitrile (31). 4-Bromobenzaldehyde (0.185 g, 1 mmol) affords **31** in 64% (0.158 g) yield; amorphous white solid; mp 231−233 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.10 (s, 1H), 8.80 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 7.93 (s, 1H), 7.80 (d, J = 9.3 Hz, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 145.8, 136.3, 135.8, 133.5, 130.9, 129.7, 128.2, 125.9, 124.6, 119.6, 116.3, 99.7. Elemental analysis calcd (%) for $C_{15}H_9N_3O$ (247.25): C 72.87, H 3.67. Found: C 72.98, H 3.54.

3-Naphthalen-2-ylimidazo[1,2-a]pyridine-6-carbonitrile (32). 2-Bromonaphthalene (0.207 g, 1 mmol) affords **32** in 72% (0.194 g) yield; amorphous white solid; mp 112−114 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H), 7.90−7.80 (m, 3H), 7.71 (d, J = 9.3 Hz, 1H), 7.60−7.50 (m, 3H), 7.25 (d, J = 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.0, 134.7, 133.4, 133.1, 129.8, 129.5, 128.0, 127.8, 127.3, 127.0, 127.1, 125.2, 124.7, 123.8, 119.2, 116.5, 98.9. Elemental analysis calcd (%) for $C_{18}H_{11}N_3$ (269.30): C 80.28, H 4.12. Found: C 80.14, H 4.00.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds and ^{1}H spectra of known compounds. This material is available free of charge via the Internet at http://pubs.acs.org

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: henri.doucet@univ-rennes1.fr.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the Chinese Scholarship Council for grants to H.Y.F. and L.C. We thank CNRS and "Rennes Metropole" for providing financial support.

■ REFERENCES

(1) (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (b) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200. (c) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (d) Li, B.-J.; Yang, S.-D.; Shi, Z.-J. *Synlett* **2008**, 949. (e) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269. (f) Ackermann, L.; Vincente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (g) Fischmeister, C.; Doucet, H. *Green Chem.* **2011**, *13*, 741.

(2) For selected recent contributions on direct arylations or vinylations of heteroaromatics from our laboratory: (a) Gottumukkala, A. L.; Derridj, F.; Djebbar, S.; Doucet, H. *Tetrahedron Lett.* **2008**, *49*, 2926. (b) Derridj, F.; Roger, J.; Djebbar, S.; Doucet, H. *Org. Lett.* **2010**, *12*, 4320. (c) Roger, J.; Požgan, F.; Doucet, H. *Adv. Synth. Catal.* **2010**, *352*, 696.

(3) (a) Akita, Y.; Inoue, A.; Yamamoto, K.; Ohta, A.; Kurihara, T.; Shimizu, M. *Heterocycles* **1985**, *23*, 2327. (b) Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuji, A.; Nakata, T.; Tani, N.; Aoyagi, Y. *Heterocycles* **1990**, *31*, 1951.

(4) Li, J. J.; Gribble, G. W. *Palladium in Heterocyclic Chemistry*; Pergamon: Amsterdam, 2000.

(5) For direct 5-arylations of heteroaromatics with aryl halides using ligand-less palladium catalysts: (a) Parisien, M.; Valette, D.; Fagnou, K. *J. Org. Chem.* **2005**, *70*, 7578. (b) Dong, J. J.; Roger, J.; Požgan, F.; Doucet, H. *Green Chem.* **2009**, *11*, 1832. (c) Roger, J.; Doucet, H. *Adv. Synth. Catal.* **2009**, *351*, 1977. (d) Roger, J.; Doucet, H. *Tetrahedron* **2009**, *65*, 9772.

(6) For examples of direct arylations at C3 of imidazo[1,2-a]pyridine: (a) Koubachi, J.; El Kazzouli, S.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. *Synlett* **2006**, 3237. (b) Touré, B. B.; Lane, B. S.; Sames, D. *Org. Lett.* **2006**, *8*, 1979. (c) Kumar, P. V.; Lin, W.-S.; Shen, J.-S.; Nandi, D.; Lee, H. M. *Organometallics* **2011**, *30*, 5160. (d) Singhaus, R. R.; Bernotas, R. C.; Steffan, R.; Matelan, E.; Quinet, E.; Nambi, P.; Feingold, I.; Huselton, C.; Wilhelmsson, A.; Goos-Nilsson, A.; Wrobel, J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 521. (e) Koubachi, J.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. *Tetrahedron* **2010**, *66*, 1937.

(7) (a) de Vries, A. H. M.; Mulders, J. M. C. A.; Mommers, J. H. M.; Henderickx, H. J. W.; de Vries, J. G. *Org. Lett.* **2003**, *5*, 3285. (b) Reetz, M. T.; de Vries, J. G. *Chem. Commun.* **2004**, 1559. (c) de Vries, J. G. *Dalton Trans.* **2006**, 421.

(8) Alimardanov, A.; Schmieder-van de Vondervoort, L.; de Vries, A. H. M.; de Vries, J. G. *Adv. Synth. Catal.* **2004**, *346*, 1812.

(9) (a) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13754. (b) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118.

(10) (a) Bensaid, S.; Laidaoui, N.; El Abed, D.; Kacimi, S.; Doucet, H. *Tetrahedron Lett.* **2011**, *52*, 1383. (b) Beydoun, K.; Doucet, H. *ChemSusChem* **2011**, *4*, 526. (c) Dong, J. J.; Roger, J.; Verrier, C.; Martin, T.; Le Goff, R.; Hoarau, C.; Doucet, H. *Green Chem.* **2010**, *12*, 2053.

(11) Byth, K. F.; Culshaw, J. D.; Green, S.; Oakes, S.; Thomas, A. P. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 2245.

(12) Liebscher, J.; Feist, K. *J. Prakt. Chem.* **1988**, *330*, 175.

(13) Wu, Z.; Pan, Y.; Zhou, X. *Synthesis* **2011**, 2255.