From the Particular Reactivity of 8-Iodoimidazo[1,2-*a*]pyridine towards Copper- and Palladium-Catalyzed Aminations

Jean-Yves Kazock,[1] Isabelle Théry,[1] Jean-Michel Chezal,[2] Olivier Chavignon,[2] Jean-Claude Teulade,[2] Alain Gueiffier,*[1] and Cécile Enguehard-Gueiffier[1]

[1]Laboratoire de Chimie Thérapeutique SPOT EA 3857, Faculté de Pharmacie, 31 avenue Monge, F-37200 Tours, France

[2]Faculté de Pharmacie UMR-INSERM 484, 28 place Henri-Dunant, BP 38, F-63001 Clermont-Ferrand Cedex 1, France

Received November 4, 2005; E-mail: alain.gueiffier@univ-tours.fr

The reactivity of 8-iodoimidazo[1,2-*a*]pyridine towards copper- and palladium-catalyzed aminations is reported. The copper-based methodology led to the attempted coupling products in only poor yields due to difficult purifications. On the contrary, good coupling yields were obtained using palladium-catalyzed amination protocols. The superiority of Pd_2dba_3 was demonstrated over $Pd(OAc)_2$.

The general 8-aminoimidazo[1,2-*a*]pyridine scaffold is currently the object of particular interest in medicinal chemistry. Lately, many patents have reported on its pharmacological properties in various biological areas. For example, **I** showed promising activities in the treatment of gastric acid related diseases,[1] while derivatives of formula **II** were described as cyclin-dependent kinase inhibitors useful in particular as antitumor agents[2] (Fig. 1). Compounds of formula **III** can be used as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors,[3] and 2-phenyl-3-(pyrimidin-4-yl)imidazo[1,2-*a*]pyridines **IV** have been prepared for treating the herpes viral infection.[4]

Due to the lack of reactivity in traditional nucleophilic substitution reactions at the 8-position in this series, compounds of formula **I** and **II** were prepared starting from 6-nitroimidazo[1,2-*a*]pyridines in two steps: reduction of the nitro group and functionalization of the 8-amino intermediates.[1,2] Preparation of compounds **III** and **IV** was described using standard pallado-catalyzed amination conditions ($Pd(OAc)_2$) starting from the 8-bromoimidazo[1,2-*a*]pyridine derivative[3] or from the 8-chlorinated starting material[4] either in poor to modest yields (10–50%), or using neat amine as a solvent (around 90% yield), wich is not a convenient synthetic approach with commercially unavailable amines.

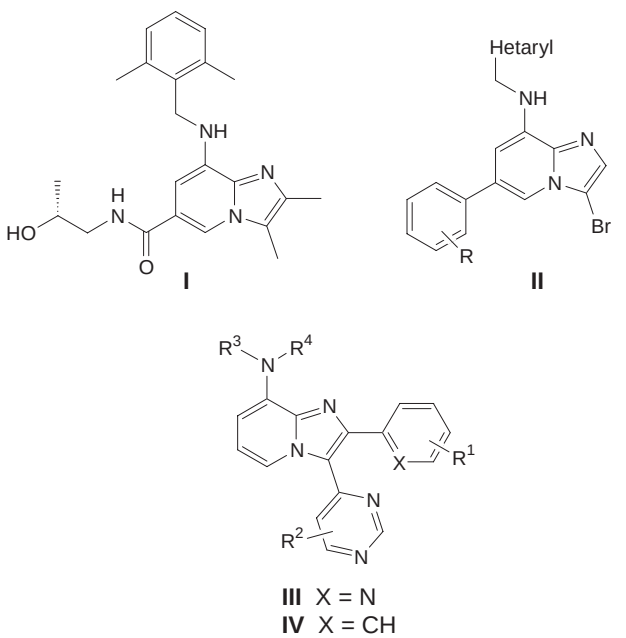

Fig. 1. 8-Aminoimidazo[1,2-*a*]pyridine derivatives with pharmacological properties.

During the course of our work to evaluate the applicability of metallo-catalyzed cross-coupling reactions in the imidazo[1,2-*a*]pyridine series,[5] we previously reported that both copper and palladium-catalyzed amination can serve as a valuable tool for the functionalization of the 6-position.[6] The copper-based C–N bond forming methodology can be carried out in mild reaction conditions and can be performed under air using an inexpensive catalyst and ligand. The limitation of this method concerns the aromatic amines that are unreactive in these catalytic conditions,[7] the palladium-based coupling being a good alternative option in this case.

Then, we felt that it would be interesting to extend the Pd- and Cu-catalyzed amination methods to the 8-position of the imidazo[1,2-*a*]pyridine series, expecting similar results as in the 6-position. Concerning the pallado-catalyzed *N*-arylation with 8-halogenoimidazo[1,2-*a*]pyridines, the two previously reported examples of the literature[3,4] have used $Pd(OAc)_2$ as the catalyst. Herein, we demonstrate the superiority of Pd_2dba_3 over $Pd(OAc)_2$ under our reaction conditions.

Results and Discussion

One of our initial forays was the investigation of the application of the copper-based methodology to the 2-(4-fluorophenyl)-8-iodo-6-methylimidazo[1,2-*a*]pyridine (**1**).[5d] The reasons for choosing this starting material were that **1** is synthesized in better yield on a large scale than the non-methyl analogue, and the 2-phenylimidazo[1,2-*a*]pyridines are more stable than the 2-unsubstituted analogues. Moreover, we have

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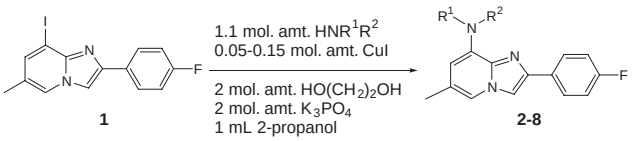
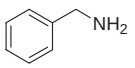
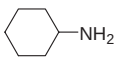
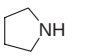
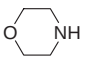
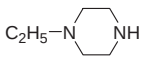
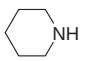
Table 1. Copper-Catalyzed Amination of 2-(4-Fluorophenyl)-8-iodo-6-methylimidazo[1,2-*a*]pyridine (**1**) with Various Amines[a)]



1 **2-8**

HNR^1R^2	Catalyst /10^{-2} mol. amt.	Temp /°C	Time /h	Product	Yield /%[b)]
	5	85	20	**2**	62
	15	85	20		31
	5	85	20	**3**	42
	15	85	20		NI[c)]
	15	85	48		48
	5	112	20		57
	15	85	20	**4**	60
	15	85	48		50
	5	112	20		49
	5	85	20	**5**	36
	15	85	20		32
	15	85	48		41
	5	112	20		55
	15	112	20		41
	5	85	20	**6**	traces
	15	85	20		24
	15	85	48		69
	5	112	20		46
	15	112	20		48
	15	85	20	**7**	23
	15	85	48		64
$nC_6H_{13}NH_2$	15	85	20	**8**	26
	15	85	48		34
	5	112	20		30

a) Reaction conditions: 1 mmol of **1**, 1.1 mmol of amine, 0.05–0.15 mol. amt. CuI, 2 mmol of ethylene glycol, 2 mmol of K_3PO_4, 1 mL of 2-propanol. b) Isolated yields. c) NI = not isolated.

already demonstrated in a previous publication that the 2-substituent has no effect on the reactivity of the 8-position.[5d] Our studies begun using the reaction conditions previously described.[6] For example, the coupling reaction of benzylamine with **1** was carried out in the presence of 0.05 molar amount of copper(I) iodide, 2 molar amounts of ethylene glycol, and 2 molar amounts of K_3PO_4 in 2-propanol (1 mL mmol^{-1}) at 85 °C for 20 h (Table 1). Using this protocol, compound **2** was obtained in 62% yield after purification was made difficult due to the presence of remaining starting material, reduced **1**, and 6-[(2-hydroxy)ethoxy]-2-(4-fluorophenyl)-6-methylimidazo[1,2-*a*]-pyridine resulting from the coupling of **1** with ethylene glycol. We encountered the same problem with compounds **3**, **5**, and **6**, which were obtained in poor yields (traces to 42%). Considering these results and the slow rate of reaction, we tried to increase the quantity of CuI from 0.05 to 0.15 molar amounts while maintaining the reaction temperature at 85 °C without success for compounds **2**, **3**, **5**, and **8**, regardless of the reaction time (20 or 48 h). Only compounds **4**, **6**, and **7** could be obtained in moderate yields, 60 to 69%, after 20 or 48 h of heating. We next tried to optimize the process at a higher reaction temperature (112 °C). A moderate increase of the coupling yield was observed for compounds **3** and **5** in the presence of 0.05 molar amount of CuI. Finally, the same purification problems were encountered using 0.15 molar amount of CuI after 20 h at 112 °C leading to poor yields of the desired compounds **5** and **6**. It appeared that increasing the CuI ratio also supports the formation of the coupling product of **1** with ethylene glycol.

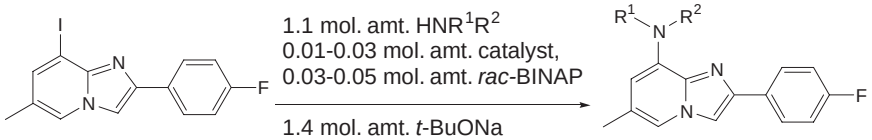
Then, we evaluated the palladium-catalyzed amination protocols as a valuable alternative to the copper-based methodology. In the first stage, $Pd(OAc)_2$ was tested according to the examples reported in the literature.[3,4] We began by using traditional reaction conditions (1.1 molar amount of amine, 0.01 molar amount of $Pd(OAc)_2$, 0.03 molar amount of *rac*-BINAP, 1.4 molar amount of *t*-BuONa/2 mL of toluene, and 20 h)[8] and applied them to the coupling of the same various amines to **1**. As far as cyclohexylamine and pyrrolidine are concerned, these initial conditions provided the coupling products **3** and **4** in good yields, 82 and 85%, respectively. The other coupling reactions led to the attempted products in moderate yields (26 to 48%). Beside the desired products, significant amounts of starting material were recovered at the end of the reaction; thus, we decided to prolong the reaction time. After 48 h of heating, compounds **2** and **9** were obtained in good yields (86%). Nevertheless, these reaction conditions remained ineffective in the cases of morpholine, *N*-ethylpiperazine, and hexylamine couplings.

As far as morpholine coupling was concerned, different alternatives were then examined: the increase of the catalyst and ligand amounts, the increase of the amine ratio, or the combination of both methods. From the different results obtained, the best conditions of morpholine coupling were 0.01 molar amount of $Pd(OAc)_2$, 0.03 molar amount of *rac*-BINAP, 1.4 molar amount of *t*-BuONa, and 1.5 molar amount of morpholine (62% yield). The improvement achieved from the use of higher amounts of catalyst and ligand (69% yield) was not significant.

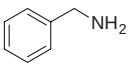
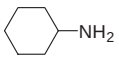
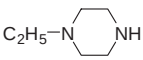
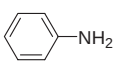
Thus, in the second stage, we decided to evaluate the efficiency of Pd_2dba_3 as catalyst, according to our previously reported method at the 6-position of the imidazo[1,2-*a*]pyridine. As shown in Table 2, benzylamine, cyclohexylamine, pyrrolidine, hexylamine, and aniline were combined with **1** leading to compounds **2**–**4**, **8**, and **9** in good yields (80 to 94%). In contrast, only moderate yields were obtained with the secondary cyclic amines, morpholine (58%), and *N*-ethylpiperazine (31% as the best yield of two experiments). We found that the coupling of morpholine with **1** was improved using 1.5 molar amount of amine giving **5** in 90% yield.

In conclusion, unlike the 6-position, no convenient copper-catalyzed reaction conditions were defined for the amination of the 8-position in the imidazo[1,2-*a*]pyridine series. The coupling products isolated with difficulty, were obtained in poor yields. The presence of a side product resulting from the coupling with ethylene glycol and of dehalogenated compound is responsible for the purification problems encountered. Moreover, the lower efficiency of the copper-based methodology on

Table 2. Palladium-Catalyzed Amination of 2-(4-Fluorophenyl)-8-iodo-6-methylimidazo[1,2-*a*]pyridine (**1**) with Various Amines[a)]



1 **2-6,8-9**

HNR^1R^2	[Pd]	Catalyst /10^{-2} mol. amt.	Ligand /10^{-2} mol. amt.	Time /h	Product	Yield /%[b)]
	$Pd(OAc)_2$	1	3	20	**2**	27
	$Pd(OAc)_2$	1	3	48		86
	Pd_2dba_3	1	3	20		92
	$Pd(OAc)_2$	1	3	20	**3**	82
	Pd_2dba_3	1	3	20		86
	$Pd(OAc)_2$	1	3	20	**4**	85
	Pd_2dba_3	1	3	20		80
	$Pd(OAc)_2$	1	3	20	**5**	40
	$Pd(OAc)_2$	1	3	48		53
	$Pd(OAc)_2$	1	3	20		62[c)]
	$Pd(OAc)_2$	3	5	20		51
	$Pd(OAc)_2$	3	5	20		69[c)]
	Pd_2dba_3	1	3	20		58
	Pd_2dba_3	1	3	20		90[c)]
	$Pd(OAc)_2$	1	3	20	**6**	48
	$Pd(OAc)_2$	1	3	48		54
	Pd_2dba_3	1	3	48		27–31
$nC_6H_{13}NH_2$	$Pd(OAc)_2$	1	3	20	**8**	42
	Pd_2dba_3	1	3	20		94
	$Pd(OAc)_2$	1	3	20	**9**	26
	$Pd(OAc)_2$	1	3	48		86
	Pd_2dba_3	1	3	20		81

a) Reaction conditions: 1 mmol of **1**, 1.1 mmol of amine, 0.01–0.03 mol. amt. of catalyst, 0.03–0.05 mol. amt. of *rac*-BINAP, 1.4 mol. amt. of *t*-BuONa, 2 mL of toluene. b) Isolated yields. c) Reaction was run using 1.5 mmol of amine.

the 8-position may have been due to an interaction of CuI with N(1). Thus, in this position, the palladium-catalyzed protocol remains the most effective amination method. Two different catalysts were evaluated, e.g., $Pd(OAc)_2$ and Pd_2dba_3. When good reactivity of the 8-position was observed in the presence of $Pd(OAc)_2$, no significantly different results were obtained using Pd_2dba_3, as for cyclohexylamine and pyrrolidine. Nevertheless, when a prolonged reaction time was required using $Pd(OAc)_2$ as catalyst to give the coupling product in good yield (e.g., benzylamine and aniline), Pd_2dba_3 proved to be superior, leading to the attempted product in good yield in only 20 h. A huge improvement was also observed for the *n*-hexylamine and morpholine couplings using Pd_2dba_3. Thus, in the 8-position of the imidazo[1,2-*a*]pyridine, we demonstrated the superiority of Pd_2dba_3 over $Pd(OAc)_2$. Finally, comparing the reactivities of positions 6 and 8 of the imidazo[1,2-*a*]pyridine towards palladium-catalyzed aminations led to comparable or slightly improved results in position 8 relative to position 6, except for the two cyclic secondary amines, morpholine and *N*-ethylpiperazine.

Experimental

General. Unless otherwise noted, all chemicals were used as received. 2-(4-Fluorophenyl)-8-iodo-6-methylimidazo[1,2-*a*]pyridine (**1**) was prepared according to a literature procedure.[5d] All materials were weighed in an air atmosphere. NMR spectra were run at 200 MHz (^{1}H) and 50 MHz (^{13}C) in $CDCl_3$ with chemical shifts reported relative to residual non-deuterated solvent peaks. Possible inversion of two values in the ^{13}C NMR spectra is expressed by an asterisk. Melting points were determined in a capillary apparatus and are uncorrected.

General Procedure for Cu-Catalyzed Aminations: Method A. 2-(4-Fluorophenyl)-8-iodo-6-methylimidazo[1,2-*a*]pyridine (**1**) (352 mg, 1 mmol), copper(I) iodide (9.5 mg, 0.05 mmol or 29 mg, 0.15 mmol), and potassium phosphate (425 mg, 2 mmol) were added to a screw-capped test tube. The tube was evacuated and back filled with nitrogen. Ethylene glycol (111 μL, 2 mmol), amine (1.1 mmol), and 2-propanol (1 mL) were added successively by syringe at room temperature. The tube was sealed with a Teflon-lined cap and the reaction mixture was heated at 85 or 112 °C for 20 or 48 h. After cooling to room temperature, the suspension

was diluted with dichloromethane and filtered through celite®. The solvent was removed with the aid of a rotary evaporator to give a brown residue that was purified by column chromatography.

General Procedure for Pd-Catalyzsed Aminations: Method B. 2-(4-Fluorophenyl)-8-iodo-6-methylimidazo[1,2-*a*]pyridine (**1**) (352 mg, 1 mmol), palladium diacetate (2.2 mg, 0.01 mmol or 6.7 mg, 0.03 mmol) or tris(dibenzylideneacetone)dipalladium (9.2 mg, 0.01 mmol), *rac*-BINAP (19 mg, 0.03 mmol or 31 mg, 0.05 mmol), and sodium *tert*-butanolate (135 mg, 1.4 mmol) were added to a screw-capped test tube. The tube was evacuated and back filled with nitrogen. Amine (1.1 mmol or 1.5 mmol) and toluene (2 mL) were added successively by syringe at room temperature. The tube was sealed with a Teflon®-lined cap, and the reaction mixture was heated at 112 °C for 20 or 48 h. After cooling to room temperature, the suspension was diluted with dichloromethane and filtered through celite®. The solvent was removed with the aid of a rotary evaporator to give a brown residue that was purified by column chromatography.

8-Benzylamino-2-(4-fluorophenyl)-6-methylimidazo[1,2-*a*]pyridine (2). The amination reaction was performed according to the general procedures A or B with benzylamine (120 µL, 1.1 mmol). Column chromatography on neutral alumina gel, eluting with a mixture of ether/petroleum ether (V/2V), afforded the pure product. mp 148–149 °C. ^{1}H NMR δ 7.91 (dd, 2H, J = 8.7, 5.5 Hz, F-Ph-2,6), 7.67 (s, 1H, H-3), 7.49–7.36 (m, 6H, H-5, Ph), 7.13 (t, 2H, J = 8.7 Hz, F-Ph-3,5), 5.96 (s, 1H, H-7), 5.61 (brs, 1H, NH), 4.54 (d, 2H, J = 5.8 Hz, CH_2), 2.24 (s, 3H, CH_3). ^{13}C NMR δ 162.8 (J = 245 Hz, F-Ph-4), 143.2 (C-2*), 139.1 (C-8a*), 138.9 (C-8*), 136.7 (Ph-1), 131.0 (F-Ph-1), 129.1 (Ph-3,5), 127.9 (Ph-2,6), 127.8 (J = 8 Hz, F-Ph-2,6), 127.7 (Ph-4), 123.8 (C-6), 115.9 (J = 21.5 Hz, F-Ph-3,5), 112.8 (C-5), 109.0 (C-3), 101.2 (C-7), 47.9 (CH_2), 19.2 (CH_3); Anal. Calcd for $C_{21}H_{18}FN_3$: C, 76.11; H, 5.47; N, 12.68%. Found: C, 75.89; H, 5.48; N, 12.66%.

8-Cyclohexylamino-2-(4-fluorophenyl)-6-methylimidazo[1,2-*a*]pyridine (3). The amination reaction was performed according to the general procedures A or B with cyclohexylamine (126 µL, 1.1 mmol). Column chromatography on neutral alumina, eluting with a mixture of CH_2Cl_2/petroleum ether (V/2V), afforded the pure product. mp 171–172 °C. ^{1}H NMR δ 7.91 (dd, 2H, J = 8.8, 5.5 Hz, F-Ph-2,6), 7.64 (s, 1H, H-3), 7.30 (s, 1H, H-5), 7.13 (t, 2H, J = 8.8 Hz, F-Ph-3,5), 5.97 (s, 1H, H-7), 5.34 (brs, 1H, NH), 3.40 (brs, 1H, cyhex), 2.28 (s, 3H, CH_3), 2.19 (m, 2H, cyhex), 1.85–1.34 (m, 8H, cyhex). ^{13}C NMR δ 162.8 (J = 244 Hz, F-Ph-4), 143.0 (C-2*), 139.2 (C-8a*), 135.7 (C-8*), 131.0 (F-Ph-1), 127.8 (J = 8 Hz, F-Ph-2,6), 124.0 (C-6), 115.9 (J = 21.5 Hz, F-Ph-3,5), 111.9 (C-5), 109.0 (C-3), 100.4 (C-7), 51.7 (cyhex), 33.35 (cyhex), 26.32 (cyhex), 25.55 (cyhex), 19.33 (CH_3); Anal. Calcd for $C_{20}H_{22}FN_3$: C, 74.28; H, 6.86; N, 12.99%. Found: C, 74.33; H, 6.72; N, 13.05%.

2-(4-Fluorophenyl)-6-methyl-8-(pyrrolidin-1-yl)imidazo[1,2-*a*]pyridine (4). The amination reaction was performed according to the general procedures A or B with pyrrolidine (92 µL, 1.1 mmol). Column chromatography on neutral alumina gel, eluting with a mixture of ether/petroleum ether (V/2V), afforded the pure product. mp 170–171 °C. ^{1}H NMR δ 7.94 (dd, 2H, J = 8.8, 5.5 Hz, F-Ph-2,6), 7.65 (s, 1H, H-3), 7.35 (s, 1H, H-5), 7.12 (t, 2H, J = 8.8 Hz, F-Ph-3,5), 5.86 (s, 1H, H-7), 3.86 (m, 4H, Pyr), 2.26 (s, 3H, CH_3), 2.06 (m, 4H, Pyr). ^{13}C NMR δ 162.7 (J = 243.5 Hz, F-Ph-4), 142.4 (C-2*), 140.1 (C-8*), 138.2 (C-8a*), 131.2 (F-Ph-1), 127.6 (J = 8 Hz, F-Ph-2,6), 123.6 (C-6), 115.8 (J = 21.5 Hz, F-Ph-3,5), 113.0 (C-5), 108.3 (C-3), 104.1 (C-7), 50.4 (Pyr), 25.8 (Pyr), 19.0 (CH_3); Anal. Calcd for $C_{18}H_{18}FN_3$: C, 73.20; H, 6.14; N, 14.23%. Found: C, 73.38; H, 6.12; N, 14.51%.

2-(4-Fluorophenyl)-6-methyl-8-morpholinoimidazo[1,2-*a*]pyridine (5). The amination reaction was performed according to the general procedures A or B with morpholine (96 µL, 1.1 mmol or 132 µL, 1.5 mmol). Column chromatography on neutral alumina gel, eluting with a mixture of CH_2Cl_2/petroleum ether (2V/V), afforded the pure product. mp 157–158 °C. ^{1}H NMR δ 7.95 (dd, 2H, J = 8.8, 5.5 Hz, F-Ph-2,6), 7.69 (s, 1H, H-3), 7.61 (s, 1H, H-5), 7.13 (t, 2H, J = 8.8 Hz, F-Ph-3,5), 6.29 (s, 1H, H-7), 4.05 (m, 4H, Mor), 3.63 (m, 4H, Mor), 2.32 (s, 3H, CH_3). ^{13}C NMR δ 162.8 (J = 244.5 Hz, F-Ph-4), 143.1 (C-2*), 140.5 (C-8a*), 140.4 (C-8*), 130.8 (F-Ph-1), 127.9 (J = 8 Hz, F-Ph-2,6), 122.6 (C-6), 117.3 (C-5), 115.8 (J = 21.5 Hz, F-Ph-3,5), 110.0 (C-7), 108.3 (C-3), 67.3 (Mor), 50.3 (Mor), 19.0 (CH_3); Anal. Calcd for $C_{18}H_{18}FN_3O$: C, 69.44; H, 5.83; N, 13.50%. Found: C, 69.61; H, 5.91; N, 13.43%.

8-(4-Ethylpiperazin-1-yl)-2-(4-fluorophenyl)-6-methylimidazo[1,2-*a*]pyridine (6). The amination reaction was performed according to the general procedures A or B with *N*-ethylpiperazine (140 µL, 1.1 mmol). Column chromatography on neutral alumina gel, eluting with CH_2Cl_2, afforded the pure product. mp 94–95 °C. ^{1}H NMR δ 7.95 (dd, 2H, J = 8.8, 5.5 Hz, F-Ph-2,6), 7.68 (s, 1H, H-3), 7.58 (s, 1H, H-5), 7.12 (t, 2H, J = 8.8 Hz, F-Ph-3,5), 6.28 (s, 1H, H-7), 3.70 (m, 4H, Pip), 2.84 (m, 4H, Pip), 2.60 (q, 2H, J = 7.2 Hz, CH_2), 2.31 (s, 3H, CH_3), 1.22 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR δ 162.8 (J = 244 Hz, F-Ph-4), 143.0 (C-2*), 140.7 (C-8a*), 140.5 (C-8*), 130.9 (F-Ph-1), 127.8 (J = 7.5 Hz, F-Ph-2,6), 122.7 (C-6), 117.0 (C-5), 115.8 (J = 21 Hz, F-Ph-3,5), 110.2 (C-7), 108.2 (C-3), 53.0 (Pip), 52.9 (CH_2), 49.7 (Pip), 19.0 (CH_3), 12.3 (CH_3); Anal. Calcd for $C_{20}H_{23}FN_4$: C, 70.98; H, 6.85; N, 16.56%. Found: C, 71.03; H, 6.81; N, 16.56%.

2-(4-Fluorophenyl)-6-methyl-8-(piperidin-1-yl)imidazo[1,2-*a*]pyridine (7). The amination reaction was performed according to the general procedure A with piperidine (109 µL, 1.1 mmol). Column chromatography on neutral alumina gel, eluting with a mixture of ether/petrolum ether (2V/V), afforded the pure product. mp 156–157 °C. ^{1}H NMR δ 7.97 (dd, 2H, J = 8.7, 5.5 Hz, F-Ph-2,6), 7.66 (s, 1H, H-3), 7.55 (s, 1H, H-5), 7.12 (t, 2H, J = 8.7 Hz, F-Ph-3,5), 6.30 (s, 1H, H-7), 3.55 (m, 4H, Pip), 2.29 (s, 3H, CH_3), 1.90 (m, 4H, Pip), 1.72 (m, 2H, Pip). ^{13}C NMR δ 162.8 (J = 244 Hz, F-Ph-4), 142.9 (C-2*), 141.5 (C-8*), 140.0 (C-8a*), 130.9 (F-Ph-1), 127.9 (J = 8 Hz, F-Ph-2,6), 122.7 (C-6), 116.6 (C-5), 115.7 (J = 21 Hz, F-Ph-3,5), 110.4 (C-7), 108.2 (C-3), 51.2 (Pip), 26.2 (Pip), 25.1 (Pip), 19.0 (CH_3); Anal. Calcd for $C_{19}H_{20}FN_3$: C, 73.76; H, 6.52; N, 13.58%. Found: C, 73.91; H, 6.47; N, 13.62%.

2-(4-Fluorophenyl)-8-hexylamino-6-methylimidazo[1,2-*a*]pyridine (8). The amination reaction was performed according to the general procedures A or B with hexylamine (145 µL, 1.1 mmol). Column chromatography on neutral alumina gel, eluting with a mixture of CH_2Cl_2/petroleum ether (V/V), afforded the pure product. Oil. ^{1}H NMR δ 7.91 (dd, 2H, J = 8.8, 5.5 Hz, F-Ph-2,6), 7.63 (s, 1H, H-3), 7.31 (s, 1H, H-5), 7.13 (dd, 2H, J = 8.8 Hz, F-Ph-3,5), 5.96 (s, 1H, H-7), 5.19 (brs, 1H, NH), 3.26 (m, 2H, CH_2), 2.28 (s, 3H, CH_3), 1.79 (m, 2H, CH_2), 1.54–1.34 (m, 6H, $3CH_2$), 0.95 (t, 3H, J = 6.6 Hz, CH_3). ^{13}C NMR δ 162.8 (J = 244 Hz, F-Ph-4), 142.7 (C-2*), 138.9 (C-8a*), 136.9 (C-8*), 130.7 (F-Ph-1), 127.8 (J = 8 Hz, F-Ph-2,6), 124.2 (C-6), 115.9 (J = 21 Hz, F-Ph-3,5), 112.2 (C-5), 109.0 (C-3), 100.8 (C-7), 43.7 (CH_2), 32.1 (CH_2), 29.5 (CH_2), 27.4 (CH_2), 23.1 (CH_2), 19.3 (CH_3), 14.5 (CH_3); Anal. Calcd for $C_{20}H_{24}FN_3$: C, 73.82; H, 7.43; N, 12.91%. Found: C, 74.01; H, 7.52; N, 12.87%.

8-Anilino-2-(4-fluorophenyl)-6-methylimidazo[1,2-*a*]pyridine (9). The amination reaction was performed according to the general procedure B with aniline (100 μL, 1.1 mmol). Column chromatography on neutral alumina gel, eluting with a mixture of ether/petrolum ether (V/2V), afforded the pure product. mp 133–134 °C. ^{1}H NMR δ 7.95 (dd, 2H, J = 8.6, 5.6 Hz, F-Ph-2,6), 7.71 (s, 1H, H-3), 7.47–7.35 (m, 4H, H-5, Ph-3,4,5), 7.24–7.08 (m, 4H, Ph-2,6, F-Ph-3,5), 6.76 (s, 1H, H-7), 2.29 (s, 3H, CH_3), 2.05 (brs, 1H, NH). ^{13}C NMR δ 163.0 (J = 245 Hz, F-Ph-4), 143.2 (C-2*), 141.2 (C-8*), 139.2 (C-8a*), 132.6 (Ph-1), 130.4 (F-Ph-1), 129.8 (Ph-3,5), 127.9 (J = 8 Hz, F-Ph-2,6), 123.7 (C-6), 123.2 (Ph-4), 120.9 (Ph-2,6), 116.1 (J = 21.5 Hz, F-Ph-3,5), 114.5 (C-5), 109.2 (C-3), 104.1 (C-7), 19.22 (CH_3); Anal. Calcd for $C_{20}H_{16}FN_3$: C, 75.69; H, 5.08; N, 13.24%. Found: C, 75.65; H, 5.09; N, 13.27%.

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