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Pd-catalyzed regiocontrolled Sonogashira and Suzuki cross-coupling reaction of 3,6-dihalogenoimidazo[1,2-*a*]pyridines: one-pot double-coupling approach

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ABSTRACT

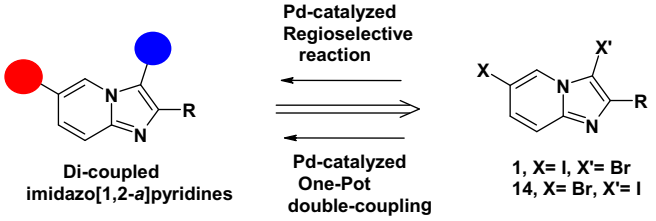
New and efficient regioselective Sonogashira and Suzuki–Miyaura palladium-catalyzed coupling reactions of 3,6-dihalogenoimidazo[1,2-*a*]pyridines followed by another cross-coupling has been successfully developed. Various solvents, palladium species and bases were tested. Scope and limitations of this regiocontrolled palladium-catalyzed reaction were investigated. The synthesis of 3,6-disubstituted imidazo[1,2-*a*]pyridine derivatives using one-pot regioselective double-coupling approach was developed. This procedure affords convergent syntheses of polysubstituted compounds in high yields in a very few steps.

1. Introduction

Palladium(0)-catalyzed carbon–carbon (Csp^2–Csp^2) bond-forming processes are widely used in synthetic chemistry.[1] Sonogashira[2] and Suzuki–Miyaura[3] cross-coupling reactions have found extensive use in natural products synthesis and for the construction of complex molecules.[4] Recently, many examples of regioselective Sonogashira and Suzuki–Miyaura[5] palladium-catalyzed reactions were described, but never in the context of imidazo[1,2-*a*]pyridines. Conducting more than one coupling in the same reaction vessel is quite rare.[6] Within the area of heteroaromatic systems, palladium is often used to catalyze single reactions. The use of alkynes as reactants in one-pot Sonogashira–Sonogashira couplings was not investigated with (hetero)aromatic systems excepted for multiple Sonogashira reactions of hexa- and pentachlorobenzene.[7]

In a previous paper, we described the regioselective palladium insertion at the position 3 of imidazo[1,2-*b*]pyridazines.[8] Our aim was to improve the efficiency of cross-coupling chemistry for the preparation of polysubstituted bicyclic heterocycles with a bridgehead nitrogen atom.[9] This initial approach was further investigated and applied to the regioselective Sonogashira and Suzuki–Miyaura palladium-catalyzed reactions of 3,6-dihalogenoimidazo[1,2-*a*]pyridines. We achieved selective functionalization of imidazo[1,2-*a*]pyridine derivatives into dissimilarly trisubstituted aromatic compounds, which is still a significant challenge in organic synthesis (Scheme 1). A synthesis of polysubstituted imidazo[1,2-*a*]pyridines via microwave-assisted one-pot Suzuki coupling/palladium-catalyzed heteroarylation and cyclization/Suzuki coupling/palladium-catalyzed heteroarylation was already developed by our team in order to reduce the number of steps requiring separation.[10]

Based on our recent study, the one-pot Suzuki–Suzuki and one-pot Sonogashira–Sonogashira cross-coupling using 3,6-dihalogenoimidazo[1,2-*a*]pyridines as starting material would be a useful method to access to desired polyfunctionalized heterocyclic precursors (Scheme 1).



Scheme 1. Convergent approach to dissimilarly 3,6-disubstituted imidazo [1,2-*a*] pyridines.

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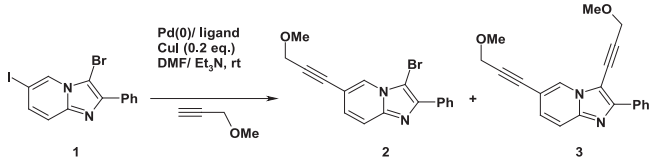
2. Results and discussion

For initial exploration, we chose 6-iodo-3-bromoimidazo[1,2-*a*]pyridine **1** then 6-bromo-3-iodoimidazo[1,2-*a*]pyridine **14** as model system (Scheme 1).

2.1. Sonogashira cross-coupling on compound 1

Initial work focused on the optimization of the first Sonogashira coupling reaction conditions to improve the reaction yield of desired monosubstituted compound without generation of symmetrical bis-alkynyl product. A model reaction was carried out with 6-iodo-3-bromoimidazo[1,2-*a*]pyridine **1** and methyl propargyl ether (1.1 equiv) under standard conditions using $PdCl_2(PPh_3)_2$ (0.05 equiv) and CuI (0.2 equiv) in a mixture of DMF/Et_3N at room temperature for 24 h.[9] In this case, compound **2** was obtained in only 74% yield (8% of starting material was recovered). Total conversion was observed with 1.3 equiv of methyl propargyl ether under the same reaction conditions and desired product **2** was generated in 92% yield (Table 3, entry 2). Influence of the Pd-catalysts on the regioselective Sonogashira cross-coupling reaction was studied. Replacement of $PdCl_2(PPh_3)_2$ by $Pd(PPh_3)_4$ afforded compound **2** and by-product **3** in 90% and 3% yield, respectively (Table 3, entry 3). [$Pd(OAc)_2$ (0.05 equiv)/PPh_3(0.1 equiv)] catalytic system used under the same reaction conditions provided compound **2** and **3** in 88% and 8% yields, respectively (Table 3, entry 4).

Table 1
Optimization of regioselective Sonogashira cross-coupling on 2-phenylimidazo[1,2-*a*]pyridine **1**



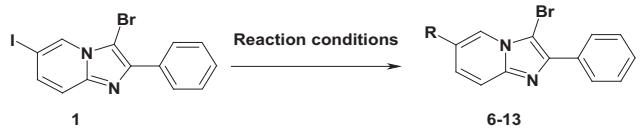
Entry	Pd(0)/ligand	Alkyne (equiv)	Time (h)	Yield[a] (%) **1**/**2**/**3**
1	$PdCl_2(PPh_3)_2$ (0.05 equiv)	1.1	24	8/74/0
2	$PdCl_2(PPh_3)_2$ (0.05 equiv)	1.3	4	0/92/0
3	$Pd(PPh_3)_4$ (0.05 equiv)	1.3	3	0/90/3
4	$Pd(OAc)_2$(0.05 equiv)/PPh_3 (0.1 equiv)	1.3	4	0/88/8

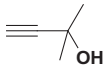
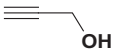
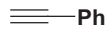
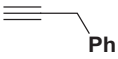
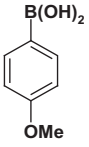
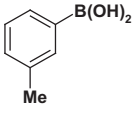
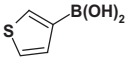
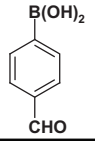
[a] Yields are given as isolated products.

2.2. Suzuki cross-coupling on compound 1 (exploration of the potential of regioselective Suzuki reaction)

6-Iodo-3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1** was treated with 3-methoxyphenylboronic acid (1.2 equiv) in the presence of $Pd(PPh_3)_4$ (0.1 equiv) and NaOH (2 equiv) in a mixture of DME/H_2O[9d] at 80 °C for 2 h. Desired monocoupled compound **4** and the dicoupled **5** were isolated in 70% and 19% yield, respectively (Table 2, entry 1). Interestingly, desired compound **4** was obtained in 90% yield when using $Pd(OAc)_2$(0.1 equiv)/PPh_3(0.2 equiv) and K_2CO_3 (2 equiv) in DMF at 100 °C with no trace of compound **5** (Table 2, entry 2).

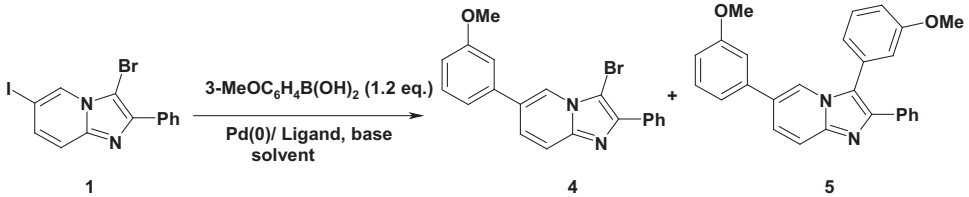
Table 3
Regioselective Sonogashira and Suzuki cross-coupling on imidazo[1,2-*a*]pyridine **1**



Entry	R	Product N°	Yield[a] (%)
1		**6**	95[b]
2		**7**	93[b]
3		**8**	91[b]
4		**9**	94[b]
5		**10**	88[c]
6		**11**	87[c]
7		**12**	90[c]
8		**13**	85[c]

[a] Yields are given as isolated products.
[b] Alkyne (1.3 equiv), $PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.2 equiv), DMF/Et_3N, rt, 2–3 h.
[c] $RB(OH)_2$ (1.2 equiv), K_2CO_3 (2 equiv), $Pd(OAc)_2$ (0.1 equiv)/PPh_3 (0.2 equiv) in DMF at 100 °C, 2 h.

Table 2
Optimization of regioselective Suzuki cross-coupling on 2-phenylimidazo[1,2-*a*]pyridine **1**



Entry	Pd(0)/ligand	Base (2 equiv)	Solvent	*T*°C/time (h)	Yield[a] (%) **1**/**4**/**5**
1	$Pd(PPh_3)_4$(0.1 equiv)	NaOH	H_2O/DME	Reflux/2	0/70/19
2	$Pd(OAc)_2$ (0.1 equiv)/PPh_3(0.2 equiv)	K_2CO_3	DMF	100/2	0/90/0

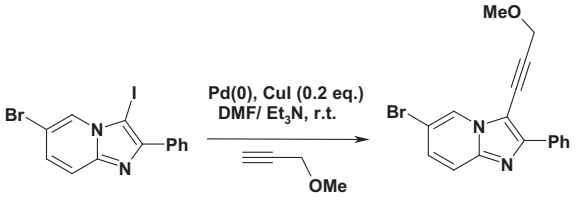
[a] Yields are given as isolated products.

The above method was applied to the synthesis of various 3-bromo-6-substituted-2-phenylimidazo[1,2-*a*]pyridine analogues. Reaction of starting material **1** with various alkynes and (hetero) arylboronic acids using our optimized conditions led to compounds **6** to **13** in excellent yields (Table 3, entries 1–7). Quantitative conversion into the corresponding monosubstituted imidazo[1,2-*a*] pyridine compounds was always observed.

2.3. Sonogashira cross-coupling on compound 14 (use of 6-bromo-3-iodo-2-phenylimidazo[1,2-*a*]pyridine 14 in Sonogashira and Suzuki–Miyaura reactions)

A first attempt of Sonogashira cross-coupling under optimized reaction conditions (Table 1, entry 2) afforded desired compound **15** in 74% yield along with some starting material **14**, which was recovered (Table 4, entry 1). When 1.5 equiv of 3-methyl propargyl ether were used, compounds **15** and **14** were isolated in 84% and 10% yields, respectively (Table 4, entry 2). The best result was observed when 2 equiv of 3-methyl propargyl ether were used (Table 4, entry 3), affording compound **15** in 90% yield. As expected absence of the phenyl group favoured coupling because of reduced steric hindrance, compounds **17**–**20** were obtained in shorter reaction times (1–1.5 h) and lesser alkyne excesses (1.3 equiv) while preserving the yields (Scheme 2).

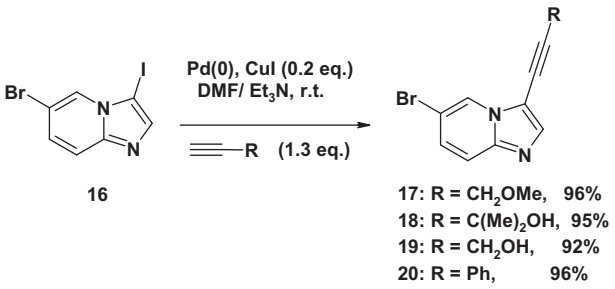
Table 4
Optimization of regioselective Sonogashira cross-coupling on imidazo[1,2-*a*]pyridine **14**



14 15

Entry	Pd(0) (0.05 equiv)	Alkyne (equiv)	Time (h)	Yield[a] (%) **14**/**15**
1	$PdCl_2(PPh_3)_2$	1.3	4	20/74
2	$PdCl_2(PPh_3)_2$	1.5	4	10/84
3	$PdCl_2(PPh_3)_2$	2	3	0/90

[a] Yields are given as isolated products.



16

17: R = CH_2OMe, 96%
18: R = $C(Me)_2OH$, 95%
19: R = CH_2OH, 92%
20: R = Ph, 96%

Scheme 2. Regioselective Sonogashira cross-coupling on 6-bromo-3-iodoimidazo[1,2-*a*]pyridine **16**.

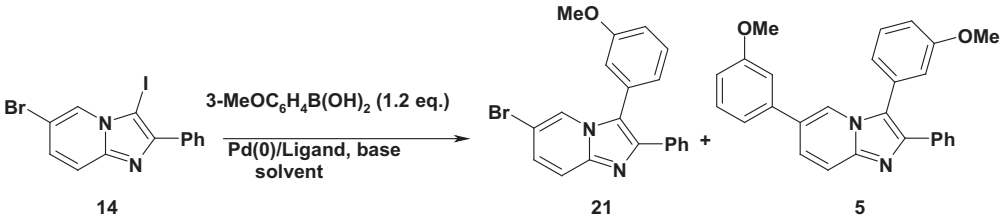
2.4. Suzuki cross-coupling on compound 14

Treatment of compound **14** under the optimized reaction conditions afforded a separable mixture of monocoupled product **21**, 3-iododerivative **14** and dicoupled product **5**, isolated in 68, 15 and 4% yield, respectively (Table 5, entry 1). Reactivity of compound **14** was studied with regards to reaction conditions, using various ligands and/or palladium species. Results are summarized in Table 5. Optimal reaction conditions were reached by using $Pd_2(dba)_3 \cdot CHCl_3$ (0.1 equiv)/$AsPh_3$(0.2 equiv) in a mixture of dioxane/EtOH at 50 °C. Under these conditions, compound **21** was obtained in 80% yield (Table 5, entry 6). Scope and limitations of regioselective Sonogashira and Suzuki cross-coupling towards imidazo[1,2-*a*]pyridine **14** were evaluated with various alkynes and (hetero)arylboronic acids, using previously optimized reaction conditions. The results show that the compound **14** was efficiently functionalized in 3-position and expected products were obtained in good yield (Table 6).

2.5. Palladium-catalyzed reaction on substituted bromocompounds

Monoarylations or monoalkynylations occurred first at the more reactive C–I position, thus leaving the remaining C–Br available for further functionalization to lead to various 3,6-disubstituted-2-phenylimidazo[1,2-*a*]pyridines. Sequential cross-coupling at C-3 of 6-substituted-3-bromo-2-phenylimidazo[1,2-*a*]pyridine and at C-6 of 6-bromo-3-substituted-2-phenylimidazo[1,2-*a*]pyridine were achieved using the same optimized catalyst systems involved in the first cross-coupling of compounds **1** and **14**. We first focused our efforts on the Suzuki approach. 3-Bromo-6-(*p*-methoxyphenyl)-2-phenylimidazo[1,2-*a*]pyridine **10** was reacted with 3-

Table 5
Optimization of regioselective Suzuki cross-coupling on imidazo[1,2-*a*]pyridine **14**

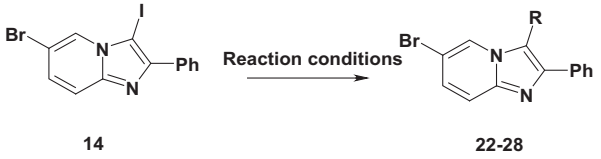


14 21 5

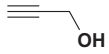
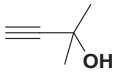
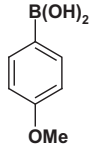
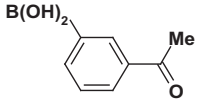
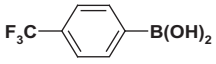
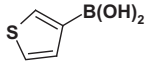
Entry	Pd(0) (0.1 equiv)/ligand (0.2 equiv)	Base (2 equiv)	Solvent	*T* (°C)/time (h)	Yield[a] (%) **14**/**21**/**5**
1	$Pd(OAc)_2/PPh_3$	K_2CO_3	DMF	100/24	15/68/4
2	$Pd(PPh_3)_4$	NaOH	H_2O/DME	Reflux/24	9/66/10
3	$PdCl_2(PPh_3)_2$	NaOH	H_2O/DME	Reflux/2	10/45/36
4	$Pd(OAc)_2/PPh_3$	K_2CO_3	DMF	50/12	20/60/0
5	$Pd(OAc)_2/PPh_3$	K_2CO_3	EtOH/dioxane	50/6	0/76/8
6	$Pd(dba)_2/AsPh_3$	K_2CO_3	EtOH/dioxane	50/12	20/64/0
7	$Pd_2(dba)_3 \cdot CHCl_3/AsPh_3$	K_2CO_3	EtOH/dioxane	50/6	0/80/0

[a] Yields are given as isolated products.

Table 6
Regioselective Sonogashira and Suzuki cross-coupling of imidazo[1,2-*a*]pyridine **14**

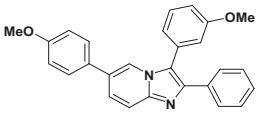
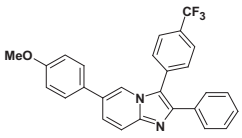
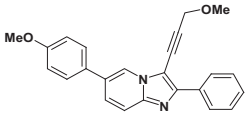
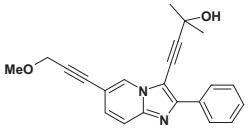
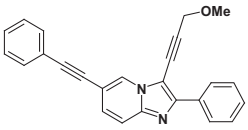


14 **22-28**

Entry	R–M (M=H, $B(OH)_2$)	N°	Yield[a] (%)
1		**22**	88[b]
2		**23**	96[b]
3		**24**	94[b]
4		**25**	82[c]
5		**26**	84[c]
6		**27**	86[c]
7		**28**	76[c]

[a] Yield are given as isolated products.
[b] Alkyne (2 equiv), $Pd(PPh_3)_4$ (0.05 equiv), CuI (0.2 equiv), DMF/Et_3N, rt, 6 h.
[c] $RB(OH)_2$ (1.2 equiv) with K_2CO_3 (2 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.1 equiv)/$AsPh_3$(0.2 equiv) in EtOH/dioxane (1/3, v/v), 50 °C, 10-12 h.

Table 7
Synthesis of dissimilarly disubstituted 2-phenylimidazo[1,2-*a*]pyridines

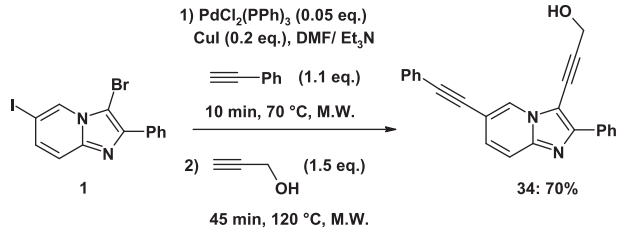
Entry	C–Br product[a]	Product N°	Yield[b] (%)
1	**10**	 **29**	63[c] 93[d]
2	**27**	 **30**	92[d]
3	**15**	 **31**	86[d]
4	**2**	 **32**	91[e]
5	**15**	 **33**	90[f]

[a] Substituted C-bromo-2-phenylimidazo[1,2-*a*]pyridines.
[b] Yields are given as isolated products.
[c] $Pd(OAc)_2$ (0.1 equiv)/PPh_3(0.2 equiv), K_2CO_3 (2 equiv), boronic acid (1.2 equiv) in DMF for 12 h, 100 °C.
[d] $Pd(OAc)_2$ (0.1 equiv)/PPh_3(0.2 equiv), K_2CO_3 (2 equiv), boronic acid (1.2 equiv) in DMF, M.W., 20 min, 140 °C.
[e] $PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.2 equiv), DMF/Et_3N (1/1, v/v), alkynes (1.5 equiv), M.W., 20 min, 140 °C.
[f] $PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.2 equiv), DMF/Et_3N (1/1, v/v), alkynes (1.3 equiv), M.W., 20 min, 140 °C.

methoxyphenylboronic acid (1.2 equiv), $Pd(OAc)_2$ (0.1 equiv), PPh_3 (0.2 equiv) and K_2CO_3 (2 equiv) in DMF at 100 °C for 12 h. These conditions allowed dissimilarly bis-arylated 2-phenylimidazo[1,2-*a*]pyridine **29** to be obtained in 63% yield (Table 7, entry 1). Microwave irradiation was tried in order to improve the yields and to decrease reaction times. We subjected the reaction mixtures of compounds **10**, **27** and **15** with several arylboronic acid (1.2 equiv) to microwave heating at 140 °C for 20 min using the already optimized reaction conditions under conventional heating [$Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %)]. This method afforded the desired compounds **29**–**31** in excellent yields (86–93%) (Table 7, entries 1–3). Then, we focused our interest on the preparation of other derivatives by Sonogashira cross-coupling performed under microwave irradiation. Treatment of compound **2** and **15** with various alkynes (1.5 equiv alkyne for compound **2** and 1.3 equiv alkyne for compound **15**) under the optimal Sonogashira conditions [$PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.2 equiv) in a mixture of DMF/Et_3N (1/1, v/v), 140 °C, 20 min, M.W.], led to compounds **32** and **33** in excellent 91% and 90% isolated yields, respectively (Table 7, entries 4 and 5). Sonogashira coupling in 3-position required 2 equiv alkyne when 6-position was halogenated, while only 1.5 equiv were necessary when 6-position was substituted by aromatic or alkyne derivative.

2.6. One-pot reaction

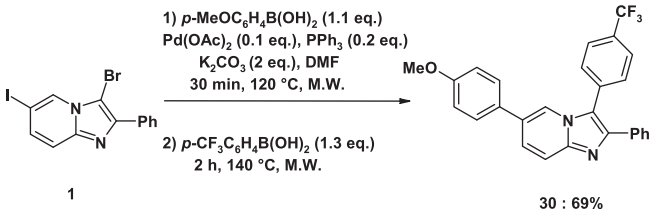
The versatility of one-pot regioselective synthesis of 3,6-disubstituted imidazo[1,2-*a*]pyridines was examined. One-pot multistep processes are economically advantageous considering the outlays for the catalyst, solvent, purification materials and time. Having successfully established the protocol to produce a mono-coupling, we shifted our focus to the one-pot bis-Sonogashira and one-pot bis-Suzuki reactions of 3,6-dihalogenoimidazo[1,2-*a*]pyridines with alkynes and (hetero)arylboronic acids (Scheme 1). Afterwards we used a single catalyst for two successive Sonogashira reactions in which a first alkyne would react selectively at the more reactive C-6 position of compound **1** then a second alkyne would be added to react at the C-3 position of compound **1** (Scheme 3). Microwave irradiation in the same pot without workup was used for that aim. The best reaction conditions were the following: 6-iodo-3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1** was treated successively with phenylacetylene (1.1 equiv only to limit mixture of compounds at second step) in the presence of $PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.2 equiv) in a mixture of DMF/Et_3N (1/1, v/v) and



Scheme 3. One-pot two-step Sonogashira–Sonogashira reaction on 6-iodo-3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1**.

was irradiated for 10 min at 70 °C (first coupling). After cooling to room temperature, propargyl alcohol (1.5 equiv) was added and the reaction mixture was irradiated again for 45 min at 120 °C (second coupling). These sequences afforded desired polysubstituted imidazo[1,2-*a*]pyridine **34** in good overall yield (70%) (Scheme 2) without side products.

One-pot two-step cross-coupling of compound **1**, with 4-methoxyphenylboronic and 4-trifluoromethylphenylboronic was also carried out. Similarly, microwave irradiation in the same pot without workup was used. The best reaction conditions were the following: 6-iodo-3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1** was treated successively with 4-methoxyphenylboronic (1.1 equiv) in the presence of $Pd(OAc)_2$ (0.1 equiv), PPh_3 (0.2 equiv), K_2CO_3 (2 equiv) in DMF and was irradiated for 30 min at 120 °C (first coupling, on iodinated position). After cooling to room temperature, 4-trifluoromethylphenylboronic (1.3 equiv) was added and the reaction mixture was irradiated again for 2 h at 140 °C (second coupling, on brominated position). These sequences afforded the desired polysubstituted imidazo[1,2-*a*]pyridine **30** in good overall yield (69%) (Scheme 4). No byproducts were detected. This approach was applied to the synthesis of dissimilarly 3,6-disubstituted-2-phenylimidazo [1,2-*a*]pyridines in a one-pot procedure. It was found that the reaction of 3,6-dihalogeno-2-phenylimidazo[1,2-*a*]pyridine **1** or **14** with various reagents **I**, followed by the addition of another reagent **II**, after completion of the first coupling (TLC monitoring), afforded the disubstituted products in good yield. Results summarized in Table 8 show a wide range of alkynyl reagents and arylboronic acids can be coupled efficiently with **1** and **14** (55–75%).



Scheme 4. One-pot two-step Suzuki–Suzuki reaction on 6-iodo-3-bromo-2-phenylimidazo[1,2-*a*]pyridine **1**.

This study provides a new and efficient regiocontrolled palladium-mediated reaction at C-iodo position of imidazo[1,2-*a*]pyridines. Conditions for generating selectively 6-bromo-3-aryl(alkynyl)-2-phenylimidazo[1,2-*a*]pyridines and 3-bromo-6-aryl(alkynyl)-2-phenylimidazo[1,2-*a*]pyridines by Pd-catalyzed regioselective Sonogashira and Suzuki–Miyaura were defined. Access to 3,6-disubstituted imidazo[1,2-*a*]pyridine with high yields using a double Sonogashira or double Suzuki–Miyaura cross-coupling reaction starting from a dihalogenoimidazo[1,2-*a*]pyridine was presented. The one-pot double-coupling reaction is useful for the synthesis of a wide range of substituted imidazo[1,2-*a*]pyridines. This method, which offers several advantages including high yields and short reaction times is currently investigated on other systems, such as imidazo[1,2-*b*]pyridazines.

3. Experimental section

3.1. General remarks and methods

All reagents were purchased from Sigma–Aldrich, Acros Organics, and Alfa Aesar and used without further purification. Microwave-assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by an IR sensor. Melting points were determined and uncorrected. ^1H and ^{13}C NMR were recorded on a spectrometer (250.19 MHz ^1H, 62.89 MHz ^{13}C) and a spectrometer (400 MHz ^1H, 100.6 MHz ^{13}C) using tetramethylsilane (TMS) as the internal standard, multiplicities were determined by the DEPT 135 sequence. Chemical shifts were reported in parts per million (ppm). Coupling constants were reported in units of hertz (Hz). Splitting patterns were designated as s, singlet, d, doublet, t, triplet, m, multiplet. High resolution mass spectra (HRMS) were recorded with a TOF spectrometer in the electrospray ionization (ESI) mode or in chemical ionization (CI) mode. All commercial solvents were used without further purification. The following solvents have been abbreviated: ethyl acetate (EtOAc), petroleum ether (PE), dimethylformamide (DMF), dimethoxyethane (DME), ethanol (EtOH). Column chromatography was carried out using Silica gel 60 N (spherical, neutral, 40–63 μm). Thin layer chromatography (TLC) was carried out on silica gel $60F_{254}$254 precoated plates. Visualization was made with UV light.

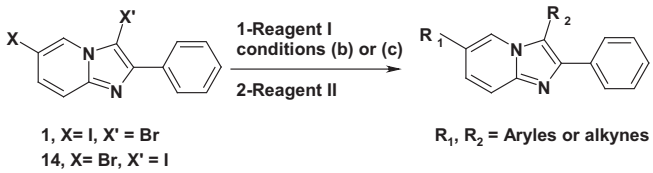
3.2. Procedure for synthesis of halogenated imidazo[1,2-*a*] pyridines 1, 14 and 16

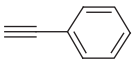
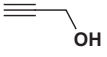
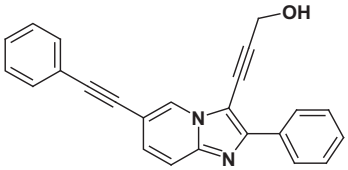
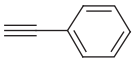
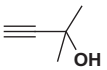
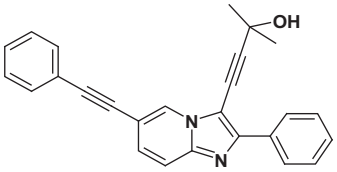
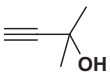
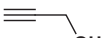
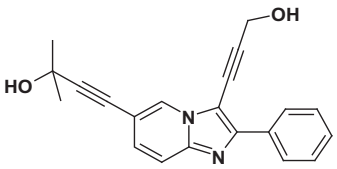
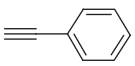
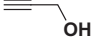
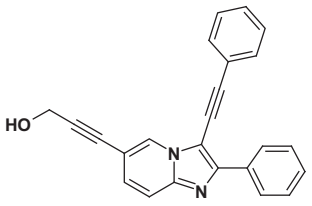
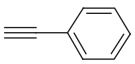
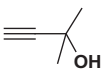
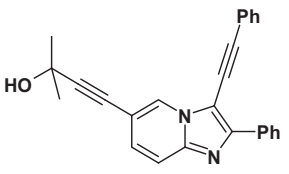
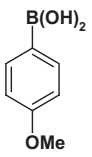
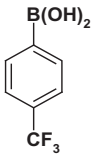
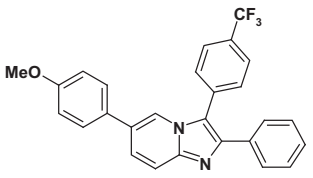
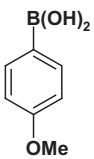
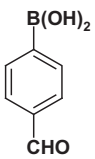
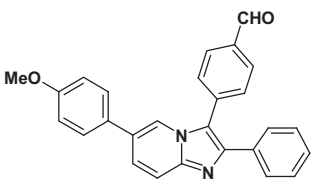
The required 6-iodo-2-phenylimidazo[1,2-*a*]pyridine, 6-bromo-2-phenylimidazo[1,2-*a*]pyridine, and 6-bromoimidazo[1,2-*a*]pyridine were prepared by condensation of the suitable 5-iodo-2-aminopyridine or 5-bromo-2-aminopyridine with 2-bromoacetophenone or chloroacetaldehyde in refluxing ethanol according to a literature procedure.[11]

*3.2.1. 3-Bromo-6-iodo-2-phenylimidazo[1,2-a]pyridine [**1**].* To a solution of 6-iodo-2-phenylimidazo[1,2-*a*]pyridine (1.0 g 3.12 mmol) in 20 mL ACN were added 667 mg (3.74 mmol) of *N*-bromosuccinimide. The reaction was stirred at room temperature for 6 h. Solvent was removed in vacuo then residue was diluted with CH_2Cl_2 and washed successively with 10% NaOH aqueous solution, saturated thiosulfate solution and then with water. The organic layer was dried over magnesium sulfate and concentrated in vacuo to afford the desired product as a white solid (1.14 g), 92% yield, mp 147–148 °C; IR (ATR) ν (cm^{-1}) 3019, 1215, 768, 696. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.44 (m, 3H), 7.47–7.49 (m, 2H), 8.11 (dd, J=5.2, 3.3 Hz, 2H), 8.42 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 76.1, 91.6, 118.6, 128.0, 128.6, 128.7, 129.1, 133.4, 133.2, 144.1. HRMS (EI) m/z calcd for $C_{13}H_8BrIN_2$ $[M]^+$: 398.8994, found: 398.8979.

*3.2.2. 6-Bromo-3-iodo-2-phenylimidazo[1,2-a]pyridine [**14**].* To a solution of 6-bromo-2-phenylimidazo[1,2-*a*]pyridine (1.0 g 3.66 mmol) in 20 mL ACN were added 988 mg (4.39 mmol) of *N*-iodosuccinimide. The reaction was stirred at room temperature for 1 h. Solvent was removed in vacuo then residue was diluted with CH_2Cl_2 and washed successively with 10% NaOH aqueous solution, saturated thiosulfate solution and then with water. The organic layer was dried over magnesium sulfate and concentrated in vacuo to afford the desired product as a white solid (1.40 g), 96% yield, mp 180–182 °C; IR (ATR) ν (cm^{-1}) 3019. 1467. 1215. 786. 695. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, J=9.4, 1.8 Hz, 1H), 7.40–7.45 (m, 1H), 7.48–7.53 (m, 3H), 8.05 (d, J=5.2 Hz, 2H), 8.38 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 108.1, 118.3, 126.8, 128.5, 128.6, 128.7, 129.1,

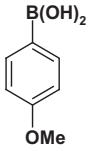
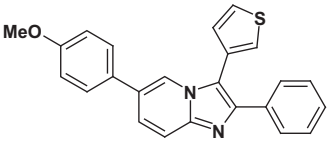
Table 8
One-pot two-step Sonogashira–Sonogashira and one-pot Suzuki–Suzuki reactions on dihalogeno-2-phenylimidazo[1,2-*a*]pyridines **1** and **14**



Entry	S.M.	Reagent **I**	Reagent **II**	Product	N°	Yield[a] (%)
1	**1**				**34**	70[b]
2	**1**				**35**	55[b]
3	**1**				**36**	68[b]
4	**14**				**37**	75[b]
5	**14**				**38**	74[b]
6	**1**				**30**	69[c]
7	**1**				**39**	71[c]

(*continued on next page*)

Table 8 (*continued*)

Entry	S.M.	Reagent **I**	Reagent **II**	Product	N°	Yield[a] (%)
8	**1**				**40**	71[c]

S.M.=starting material.

[a] Yields are given as isolated products.

[b] Reaction conditions of one-pot double Sonogashira coupling: (1) Reagent **I** (1.1 equiv), $PdCl_2(PPh_3)_2$ (0.05 equiv), CuI (0.2 equiv) DMF/Et_3N (1/1, v/v), 10 min, 70 °C, M.W. (2) Reagent **II** (1.5 equiv) 30–45 min, 140 °C, M.W.

[c] Reaction conditions of one-pot double Suzuki coupling: (1) Reagent **I** (1.1 equiv), $Pd(OAc)_2$ (0.1 equiv), PPh_3 (0.2 equiv), K_2CO_3 (2 equiv), DMF, 30 min, 120 °C, M.W. (2) Reagent **II** (1.3 equiv), 2 h, 140 °C, M.W.

133.2, 146.7, 148.9. HRMS (EI) *m*/*z* calcd for $C_{13}H_8BrIN_2$ $[M]^+$: 398.8994, found: 398.8986.

*3.2.3. 6-Bromo-3-iodoimidazo[1,2-a]pyridine [**16**].* To a solution of 6-bromoimidazo[1,2-*a*]pyridine (721 mg 3.66 mmol) in 20 mL ACN were added 988 mg (4.39 mmol) of *N*-iodosuccinimide. The reaction was stirred at room temperature for 1 h. Solvent was removed in vacuo then residue was diluted with CH_2Cl_2 and washed successively with 10% NaOH aqueous solution, saturated thiosulfate solution and then with water. The organic layer was dried over magnesium sulfate and concentrated in vacuo to afford the desired product as a white solid (1.18 g), 96% yield, mp 209 °C; IR (ATR) ν (cm^{-1}) 3024. 1516. 711. 698. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J*=9.6, 1.8 Hz, 1H), 7.51 (d, *J*=9.6 Hz, 1H), 7.70 (s, 1H), 8.26–8.28 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 61.4, 108.4, 118.6, 126.4, 128.6, 128.6, 141.1, 146.5. HRMS (EI) *m*/*z* calcd for $C_7H_4BrIN_2$ $[M+H]^+$: 322.8675, found: 322.8678.

3.3. Procedure for Sonogashira cross-coupling reaction of imidazo[1,2-*a*]pyridine [1]

To a solution of 3-iodo-6-bromophenylimidazo[1,2-*a*]pyridine **1** (100 mg 0.250 mmol) in 2 mL of a mixture of DMF/Et_3N (1/1, v/v) were added 9.5 mg (0.050 mmol) of copper iodide, alkyne (0.325 mmol) and 8.7 mg (0.012 mmol) of bis(triphenylphosphine) palladium dichloride. The reaction was stirred at room temperature sealed under argon. Once TLC indicated complete consumption of starting material (4 h), the reaction was quenched with water and extracted with dichloromethane (2×15 mL). The combined organic layers were dried over magnesium sulfate and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (EtOAc/PE) to afford the corresponding cross-coupling products **2**, **3**, **6**, **7**, **8** and **9**.

*3.3.1. 3-Bromo-6-(3-methoxyprop-1-ynyl)-2-phenylimidazo-[1,2-a] pyridine [**2**].* Yellow solid, 92% yield, mp 92 °C; IR (ATR) ν (cm^{-1}) 3026, 2988, 2360, 1445, 1318, 1092, 820, 768, 689. ^1H NMR (400 MHz, $CDCl_3$) δ 3.44 (s, 3H), 4.31 (s, 2H), 7.20–7.25 (m, 1H), 7.33–7.39 (m, 1H), 7.42–7.46 (m, 2H), 7.53 (d, *J*=9.2 Hz, 1H), 8.06–8.11 (m, 2H), 8.25 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 58.0, 60.4, 82.4, 87.1, 109.4, 117.3, 127.2, 127.5, 127.9, 128.0, 128.6, 128.6, 132.5, 143.6, 144.4. HRMS (EI) *m*/*z* calcd for $C_{17}H_{13}BrN_2O$ $[M]^+$: 341.0289, found: 341.0278.

*3.3.2. 3,6-Bis-(3-methoxyprop-1-ynyl)-2-phenylimidazo[1,2-a]pyridine [**3**].* Brown oil; IR (ATR) ν (cm^{-1}) 2988, 1449, 1090, 820. ^1H NMR (400 MHz, $CDCl_3$) δ 3.48 (s, 3H), 3.52 (s, 3H), 4.34 (s, 2H), 4.55 (s, 2H), 7.25 (dd, *J*=8.7, 1.6 Hz, 1H), 7.37 (td, *J*=4.7, 1.2 Hz, 1H), 7.44–7.50 (m, 2H), 7.55 (dd, *J*=9.2, 0.8 Hz, 1H), 8.24–8.27 (m, 2H), 8.43 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 57.9, 58.0, 60.4, 60.8, 75.1, 82.4, 87.1, 98.2, 104.3, 109.3, 117.2, 127.3, 128.3, 128.6, 128.9, 129.2, 133.0, 144.1, 149.2. HRMS (EI) *m*/*z* calcd for $C_{21}H_{18}N_2O_2$ $[M+H]^+$: 331.1447, found: 331.1430.

*3.3.3. 4-(3-Bromo-2-phenylimidazo[1,2-a]pyridin-6-yl)-2-methylbut-3-yn-2-ol [**6**].* White solid, 95% yield, mp 152 °C; IR (ATR) ν (cm^{-1}) 3280, 2974, 2361, 1444, 1219, 810, 769, 689. ^1H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 6H), 2.53–2.86 (m, 1H), 7.15–7.19 (m, 1H), 7.34–7.42 (m, 1H), 7.45–7.48 (m, 2H), 7.56 (d, *J*=9.2 Hz, 1H), 8.07–8.15 (m, 2H), 8.16–8.22 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.5, 65.6, 78.1, 92.1, 96.0, 117.3, 125.5, 126.8, 128.0, 128.2, 128.6, 128.7, 132.5, 143.5, 144.4. HRMS (EI) *m*/*z* calcd for $C_{18}H_{15}BrN_2O$ $[M]^+$: 355.0446, found: 355.0432.

*3.3.4. 3-(3-Bromo-2-phenylimidazo[1,2-a]pyridin-6-yl)-prop-2-yn-1-ol [**7**].* White solid, 93% yield, mp 186 °C; IR (ATR) ν (cm^{-1}) 3244, 2984, 2360, 1440, 1032, 816, 688. ^1H NMR (400 MHz, DMSO-d_6) δ 4.36 (d, *J*=5.8 Hz, 2H), 5.43 (t, *J*=5.8 Hz, 1H), 7.33–7.33 (m, 1H), 7.42 (dd, *J*=8.3, 6.3 Hz, 1H), 7.49–7.52 (m, 2H), 7.67 (d, *J*=9.2 Hz, 1H), 8.05–8.10 (m, 2H), 8.43–8.47 (m, 1H). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 49.3, 79.7, 91.5, 109.0, 117.1, 126.9, 127.2, 127.9, 128.5, 128.6, 132.2, 141.9, 142.1, 143.6. HRMS (EI) *m*/*z* calcd for $C_{16}H_{11}BrN_2O$ $[M]^+$ 327.0133, found: 327.0115.

*3.3.5. 3-Bromo-2-phenyl-6-(phenylethynyl)imidazo[1,2-a]pyridine [**8**].* White solid, 91% yield, mp 130 °C; IR (ATR) ν (cm^{-1}) 3024, 2360, 1538, 1415, 1222, 824, 755, 687. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.42 (m, 5H), 7.47–7.51 (m, 2H), 7.55–7.50 (m, 2H), 7.59 (d, *J*=9.2 Hz, 1H), 8.09–8.16 (m, 2H), 8.27–8.41 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 85.3, 91.4, 110.2, 117.4, 122.5, 126.7, 127.6, 128.0, 128.2, 128.6, 128.6, 128.7, 128.9, 131.7, 132.6, 143.6, 144.4. HRMS (EI) *m*/*z* calcd for $C_{21}H_{13}BrN_2$ $[M]^+$: 373.0340, found: 373.0328.

*3.3.6. 3-Bromo-2-phenyl-6-(3-phenylprop-1-ynyl)imidazo[1,2-a] pyridine [**9**].* White solid, 94% yield, mp 125 °C; IR (ATR) ν (cm^{-1}) 3027, 2362, 1415, 768, 696, 686. ^1H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 2H), 7.23–7.31 (m, 2H), 7.34–7.43 (m, 5H), 7.45–7.49 (m, 2H), 7.55 (dd, *J*=9.2, 0.7 Hz, 1H), 8.08–8.14 (m, 2H), 8.29 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 25.9, 78.6, 89.9, 110.4, 117.2, 126.7, 127.0, 127.8, 127.9, 128.1, 128.5, 128.5, 128.6, 128.8, 132.7, 136.2, 143.4, 144.4. HRMS (EI) *m*/*z* calcd for $C_{22}H_{15}BrN_2$ $[M]^+$: 387.0497, found: 387.0484.

3.4. Procedure for Suzuki cross-coupling reaction of imidazo [1,2-*a*]pyridine [1]

To a solution of 6-iodo-3-bromophenylimidazo[1,2-*a*]pyridine **1** (100 mg 0.250 mmol) in 2 mL of DMF were successively added the desired (het)Ar boronic acid (0.300 mmol), potassium carbonate (0.501 mmol), triphenylphosphine (0.050 mmol) and palladium(II) acetate (0.025 mmol). The reaction was stirred at 100 °C sealed under argon. Once TLC indicated complete consumption of starting

material (2 h), the reaction was cooled to room temperature, quenched with water and extracted with dichloromethane (2×15 mL). The combined organic layers were dried over magnesium sulfate and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (EtOAc/PE) to afford the corresponding cross-coupling products **4**, **5**, **10**–**13**.

*3.4.1. 3-Bromo-6-(3-methoxyphenyl)-2-phenylimidazo[1,2-a]pyridine [**4**].* White solid, 90% yield, mp 127–128 °C; IR (ATR) ν (cm^{-1}) 1586, 1487, 1465, 1286, 825, 772, 718. ^1H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 6.95 (dd, J=8.1, 2.2 Hz, 1H), 7.10–7.14 (m, 1H), 7.19 (d, J=7.7 Hz, 1H), 7.38–7.41 (m, 2H), 7.45–7.54 (m, 3H), 7.69 (d, J=9.2 Hz, 1H), 8.11–8.17 (m, 2H), 8.33 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 92.2, 113.2, 113.3, 117.5, 119.6, 121.4, 126.1, 127.7, 128.0, 128.5, 128.6, 130.4, 132.9, 138.7, 143.3, 144.9, 160.3. HRMS (EI) m/z calcd for $C_{20}H_{15}BrN_2O$ $[M]^+$: 379.0434, found: 379.0446.

*3.4.2. 3,6-Bis-(3-methoxyphenyl)-2-phenylimidazo[1,2-a]pyridine [**5**].* White solid, 19% yield, mp 140 °C; IR (ATR) ν (cm^{-1}) 1586, 1575, 1472, 1234, 1044, 776. ^1H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 3.86 (s, 3H), 6.91 (dd, J=8.1, 2.1 Hz, 1H), 7.00–7.06 (m, 3H), 7.07–7.09 (m, 2H), 7.25–7.27 (m, 1H), 7.28–7.33 (m, 2H), 7.36 (t, J=7.9 Hz, 1H), 7.44–7.47 (m, 1H), 7.48 (d, J=4.2 Hz, 1H), 7.70–7.72 (m, 2H), 7.74 (d, J=9.3 Hz, 1H), 8.12 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 112.8, 113.3, 114.9, 116.1, 117.4, 119.5, 120.8, 121.4, 123.0, 125.5, 126.8, 127.6, 128.1, 128.4, 130.2, 130.8, 131.2, 134.2, 139.2, 143.0, 144.2, 160.2, 160.6. HRMS (EI) m/z calcd for $C_{27}H_{22}N_2O_2$ $[M+H]^+$: 407.1760, found: 407.1751.

*3.4.3. 3-Bromo-6-(4-methoxyphenyl)-2-phenylimidazo[1,2-a]pyridine [**10**].* White solid, 88% yield, mp 198 °C; IR (ATR) ν (cm^{-1}) 2998, 1605, 1512, 1439, 1245, 813, 735, 700. ^1H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.01 (d, J=8.7 Hz, 2H), 7.39 (t, J=7.3 Hz, 1H), 7.46–7.48 (m, 3H), 7.52 (d, J=8.7 Hz, 2H), 7.66 (d, J=9.2 Hz, 1H), 8.14 (d, J=7.7 Hz, 2H), 8.24–8.28 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 92.0, 114.7, 117.4, 120.6, 126.0, 127.4, 127.9, 128.2, 128.4, 128.5, 129.6, 133.0, 143.1, 144.7, 159.8. HRMS (EI) m/z calcd for $C_{20}H_{15}BrN_2O$ $[M]^+$: 379.0438, found: 379.0446.

*3.4.4. 3-Bromo-6-(m-tolyl)-2-phenylimidazo[1,2-a]pyridine [**11**].* Yellow solid, 87% yield, mp 71 °C; IR (ATR) ν (cm^{-1}) 3062, 2919, 1673, 1466, 1439, 1211, 826, 730, 680. ^1H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.21–7.24 (m, 1H), 7.37–7.40 (m, 4H), 7.43–7.50 (m, 3H), 7.66 (d, J=9.2 Hz, 1H), 8.06–8.17 (m, 2H), 8.27 (d, J=0.7 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.6, 92.1, 117.5, 121.2, 124.2, 126.1, 127.8, 127.9, 128.4, 128.5, 128.9, 129.1, 133.0, 137.1, 139.0, 143.2, 144.9. HRMS (EI) m/z calcd for $C_{20}H_{15}BrN_2$ $[M]^+$: 363.0497, found: 363.0498.

*3.4.5. 3-Bromo-2-phenyl-6-(thiophen-3-yl)imidazo[1,2-a]pyridine [**12**].* Yellow solid, 90% yield, mp 191 °C; IR (ATR) ν (cm^{-1}) 1467, 1426, 1145, 775, 766, 693. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.43 (m, 2H), 7.46–7.53 (m, 5H), 7.66 (dd, J=9.2, 0.7 Hz, 1H), 8.13–8.16 (m), 8.35 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 92.2, 117.7, 120.6, 121.3, 122.7, 125.5, 125.9, 127.3, 127.9, 128.4, 128.6, 132.9, 138.0, 143.2, 144.8. HRMS (EI) m/z calcd for $C_{17}H_{11}BrN_2S$ $[M]^+$: 354.9905, found: 354.9889.

*3.4.6. 4-(3-Bromo-2-phenylimidazo[1,2-a]pyridin-6-yl)benzaldehyde [**13**].* Yellow solid, 85% yield, mp 192 °C; IR (ATR) ν (cm^{-1}) 2780, 1700, 1601, 1469, 1213, 815, 771, 695. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, J=7.3 Hz, 1H), 7.50 (t, J=7.5 Hz, 2H), 7.56 (dd, J=9.3, 1.7 Hz, 1H), 7.75 (d, J=9.2 Hz, 1H), 7.80 (d, J=8.1 Hz, 2H), 8.02 (d, J=8.1 Hz, 2H), 8.13–8.19 (m, 2H), 8.42 (s, 1H), 10.10 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 92.6, 118.0, 122.0, 125.3, 126.4, 127.7, 128.0, 128.6, 130.7, 132.7, 135.9, 143.1, 143.8, 145.0, 191.6. HRMS (EI) m/z calcd for $C_{20}H_{13}BrN_2O$ $[M]^+$: 377.0289, found: 377.0274.

3.5. Procedure for Sonogashira cross-coupling reaction of imidazo[1,2-*a*]pyridines (14 or 16)

To a solution of 6-bromo-3-iodoimidazo[1,2-*a*]pyridine (**14** or **16**) (**14**: 100 mg or **16**: 81 mg, 0.250 mmol) in 2 mL of a mixture of DMF/Et_3N (1/1, v/v) were successively added the desired alkyne (0.501 mmol), copper iodide (0.050 mmol) and 8.7 mg (0.012 mmol) of bis(triphenylphosphine)palladium dichloride. The reaction was stirred at room temperature sealed under argon. Once TLC indicated complete consumption of starting material (3 h), the reaction was quenched with water and extracted with dichloromethane (2×15 mL). The combined organic layer were dried over magnesium sulfate and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (EtOAc/PE) to afford the corresponding cross-coupling products **15**, **17**–**20**, and **22**–**24**.

*3.5.1. 6-Bromo-3-(3-methoxyprop-1-ynyl)-2-phenylimidazo-[1,2-a]pyridine [**15**].* Yellow solid, 90% yield, mp 95 °C; IR (ATR) ν (cm^{-1}) 3057, 2923, 2360, 1516, 1492, 1492, 1088, 820, 796, 687. ^1H NMR (400 MHz, $CDCl_3$) δ 3.52 (s, 3H), 4.54 (s, 2H), 7.31 (dd, J=9.4, 1.8 Hz, 1H), 7.36–7.41 (m, 1H), 7.44–7.48 (m, 2H), 7.51 (d, J=9.2 Hz, 1H), 8.25–8.26 (m, 2H), 8.39 (d, J=1.1 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 58.0, 60.7, 75.0, 98.3, 104.3, 107.9, 118.1, 125.2, 127.3, 128.6, 128.9, 129.8, 143.6, 143.6, 149.0. HRMS (EI) m/z calcd for $C_{17}H_{13}BrN_2O$ $[M]^+$: 341.0289, found: 341.0270.

*3.5.2. 6-Bromo-3-(3-methoxyprop-1-ynyl)imidazo[1,2-a]pyridine [**17**].* Yellow solid, 96% yield, mp 76 °C; IR (ATR) ν (cm^{-1}) 3063, 2208, 1479, 1310, 1088, 902, 753. ^1H NMR (400 MHz, $CDCl_3$) δ 3.49 (s, 3H), 4.47 (s, 2H), 7.33 (dd, J=9.6, 1.8 Hz, 1H), 7.55 (d, J=9.6 Hz, 1H), 7.83 (s, 1H), 8.415–8.419 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 57.9, 60.5, 73.2, 96.1, 108.2, 118.6, 125.3, 129.2, 139.2. HRMS (EI) m/z calcd for $C_{11}H_{10}BrN_2O$ $[M+H]^+$: 264.9971, found: 264.9971.

*3.5.3. 4-(6-Bromoimidazo[1,2-a]pyridin-6-yl)-2-methylbut-3-yn-2-ol [**18**].* Yellow solid, 95% yield, mp 129 °C; IR (ATR) ν (cm^{-1}) 3206, 2980, 1487, 1154, 802, 690. ^1H NMR (400 MHz, $CDCl_3$) δ 1.71 (s, 6H), 7.32 (dd, J=9.2, 1.6 Hz, 1H), 7.54 (d, J=9.2 Hz, 1H), 7.79 (s, 1H), 8.32 (dd, J=1.6, 0.8 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.6, 66.1, 69.2, 104.8, 108.2, 118.7, 125.2, 129.2, 138.7. HRMS (EI) m/z calcd for $C_{12}H_{12}BrN_2O$ $[M+H]^+$: 279.0128, found: 279.0127.

*3.5.4. 3-(6-Bromoimidazo[1,2-a]pyridin-6-yl)-prop-2-yn-1-ol [**19**].* Yellow solid, 92% yield, mp 154 °C; IR (ATR) ν (cm^{-1}) 3180, 3063, 2208, 1479, 1080, 690. ^1H NMR (400 MHz, DMSO-d_6) δ 4.46 (d, J=6.0 Hz, 2H), 5.45 (t, J=6.0 Hz, 1H), 7.51 (dd, J=9.6, 2.0 Hz, 1H), 7.67 (d, J=9.6 Hz, 1H), 7.91 (s, 1H), 8.68 (s, 1H). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 49.8, 70.6, 100.7, 107.7, 118.5, 125.3, 129.1, 138.0. HRMS (EI) m/z calcd for $C_{10}H_8BrN_2O$ $[M+H]^+$: 250.9815, found: 250.9812.

*3.5.5. 6-Bromo-3-(phenylethynyl)imidazo[1,2-a]pyridine [**20**].* Yellow solid, 96% yield, mp 122 °C; IR (ATR) ν (cm^{-1}) 3059, 2208, 1473, 1240, 684. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, J=15.2, 2.8 Hz, 1H), 7.39–7.43 (m, 3H), 7.55 (s, 1H), 7.58–7.61 (m, 2H), 7.89 (s, 1H), 8.47 (d, J=2.0 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 75.8, 99.8, 108.3, 118.8, 122.3, 125.5, 128.7, 129.1, 129.2, 131.6, 138.8. HRMS (EI) m/z calcd for $C_{15}H_{10}BrN_2$ $[M+H]^+$: 297.0022, found: 297.0025.

*3.5.6. 3-(6-Bromo-2-phenylimidazo[1,2-a]pyridin-6-yl)-prop-2-yn-1-ol [**22**].* White solid, 88% yield, mp 211 °C; IR (ATR) ν (cm^{-1}) 3183, 3082, 2972, 2360, 1491, 1088, 682. ^1H NMR (400 MHz, DMSO-d_6) δ 4.57 (d, J=6.0 Hz, 2H), 5.55 (t, J=6.0 Hz, 1H), 7.39–7.45 (m, 1H), 7.51 (t, J=7.5 Hz, 2H), 7.55 (dd, J=9.4, 1.9 Hz, 1H), 7.68 (d, J=9.4 Hz,

1H), 8.24–8.28 (m, 2H), 8.69 (d, J=1.1 Hz, 1H). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 49.8, 66.2, 71.7, 103.1, 107.5, 118.2, 125.1, 126.4, 128.6, 128.7, 129.9, 132.5, 142.8, 146.4. HRMS (EI) m/z calcd for $C_{16}H_{11}BrN_2O$ $[M]^+$: 327.0133, found: 327.0116.

3.5.7. 4-(6-Bromo-2-phenylimidazo[1,2-a]pyridin-6-yl)-2-methylbut-3-yn-2-ol ***[23]****.* White solid, 96% yield, mp 223 °C; IR (ATR) ν (cm^{-1}) 3183, 2973, 2360, 1491, 1087, 682. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.62 (s, 6H), 5.80 (s, 1H), 7.38–7.46 (m, 1H), 7.46–7.57 (m, 3H), 7.68 (dd, J=9.4, 0.7 Hz, 1H), 8.27–8.28 (m, 2H), 8.60 (dd, J=1.8, 0.8 Hz, 1H). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 31.1, 64.1, 68.8, 103.8, 107.4, 108.7, 118.0, 124.8, 126.3, 128.5, 128.6, 129.7, 132.6, 142.7, 146.3. HRMS (EI) m/z calcd for $C_{18}H_{15}BrN_2O$ $[M]^+$: 355.0446, found: 355.0431.

3.5.8. 6-Bromo-2-phenyl-3-(phenylethynyl)imidazo[1,2-a]pyridine ***[24]****.* White solid, 94% yield, mp 148 °C; IR (ATR) ν (cm^{-1}) 3021, 2360, 2201, 1473, 1319, 1246, 709, 684. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, J=9.4, 1.8 Hz, 1H), 7.36–7.43 (m, 4H), 7.46–7.49 (m, 2H), 7.53 (d, J=9.4 Hz, 1H), 7.58–7.64 (m, 2H), 8.31–8.36 (m, 2H), 8.43 (d, J=1.0 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 77.6, 101.9, 105.1, 107.8, 118.1, 122.4, 125.3, 127.3, 128.7, 128.9, 129.1, 129.7, 131.4, 133.1, 143.6, 148.5. HRMS (EI) m/z calcd for $C_{21}H_{13}BrN_2$ $[M]^+$: 373.0340, found: 373.0336.

3.6. Procedure for Suzuki cross-coupling reaction of imidazo [1,2-*a*]pyridine 14

To a solution of 3-iodo-6-bromophenylimidazo[1,2-*a*]pyridine (100 mg 0.250 mmol) in 2 mL of a mixture of 1,4-dioxane/EtOH (2/1, v/v) were successively added the desired (het)Ar boronic acid (0.300 mmol), potassium carbonate (0.501 mmol), triphenylarsine (0.050 mmol) and tris(dibenzylideneacetone)dipalladium(0)-chloroform adduct (0.025 mmol). The reaction was stirred at 50 °C sealed under argon. Once TLC indicated complete consumption of starting material (6 h), the reaction was cooled to room temperature, quenched with water and extracted with dichloromethane (2×15 mL). The combined organic layers were dried over magnesium sulfate and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (EtOAc/PE) to afford the corresponding cross-coupling products **21**, **25**–**28**.

3.6.1. 6-Bromo-3-(3-methoxyphenyl)-2-phenylimidazo[1,2-a]pyridine ***[21]****.* White solid, 80% yield, mp 144 °C; IR (ATR) ν (cm^{-1}) 1510, 1316, 1250, 779, 718, 696. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 6.95 (s, 1H), 7.01–7.06 (m, 2H), 7.23–7.29 (m, 4H), 7.46 (t, J=7.9 Hz, 1H), 7.56 (d, J=9.4 Hz, 1H), 7.67 (d, J=8.0 Hz, 2H), 8.04–8.09 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.4, 107.1, 115.0, 116.0, 118.2, 121.3, 122.9, 123.5, 127.8, 128.0, 128.4, 130.5, 130.9, 133.7, 143.2, 160.6. HRMS (EI) m/z calcd for $C_{20}H_{15}BrN_2O$ $[M]^+$: 379.0446, found: 379.0428.

3.6.2. 6-Bromo-3-(4-methoxyphenyl)-2-phenylimidazo[1,2-a]pyridine ***[25]****.* White solid, 82% yield, mp 142 °C; IR (ATR) ν (cm^{-1}): 1511, 1479, 1250, 1032, 697. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 6.96 (dd, 1H, J=8.1, 2.2 Hz), 7.12–7.15 (m, 1H), 7.19 (d, 1H, J=7.6 Hz), 7.39–7.43 (m, 2H), 7.46–7.54 (m, 3H), 7.70 (d, 1H, J=9.3 Hz), 8.11–8.17 (m, 2H), 8.33 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 92.2, 113.2, 113.3, 117.5, 119.6, 121.4, 126.1, 127.7, 128.0, 128.5, 128.6, 130.4, 132.9, 138.7, 143.3, 144.9, 160.3. HRMS (EI) m/z calcd for $C_{20}H_{15}BrN_2O$ $[M]^+$: 379.0446, found: 379.0426.

3.6.3. 1-[3-(6-Bromo-2-phenylimidazo[1,2-a]pyridin-3-yl)-phenyl] ethanone ***[26]****.* Yellow solid, 84% yield, mp 152 °C; IR (ATR) ν (cm^{-1}) 3017, 2360, 1685, 1497, 1232, 809, 695. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 3H), 7.23–7.27 (m, 4H), 7.55–7.65 (m, 5H), 7.98 (dd, J=1.7, 0.7 Hz, 1H), 8.01 (dd, J=1.7, 0.7 Hz, 1H), 8.07 (td, J=7.1, 1.8 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.8, 107.5, 118.5, 120.3, 123.2, 128.1, 128.1, 128.5, 128.5, 129.1, 130.0, 130.3, 130.5, 133.4, 135.4, 138.6, 143.5, 143.9, 197.4. HRMS (EI) m/z calcd for $C_{21}H_{15}BrN_2O$ $[M]^+$: 391.0446, found: 391.0431.

3.6.4. 6-Bromo-2-phenyl-3-(4-trifluorométhylphenyl)imidazo-[1,2-a]pyridine ***[27]****.* Brown solid, 86% yield, mp 192 °C; IR (ATR) ν (cm^{-1}) 1492, 1390, 1331, 1116, 1102, 1068, 826, 695. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.33 (m, 4H), 7.51–7.61 (m, 5H), 7.79 (d, J=8.06 Hz, 2H), 8.06 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 107.6, 118.5, 119.9, 123.1, 126.7, 126.7, 126.8, 126.8, 128.2, 128.3, 128.6, 128.6, 131.0, 131.0, 133.1, 133.3, 143.7, 144.3. HRMS (EI) m/z calcd for $C_{20}H_{12}BrF_3N_2$ $[M]^+$: 417.0214, found: 417.0203.

3.6.5. 6-Bromo-2-phenyl-3-(thiophen-3-yl)imidazo[1,2-a]pyridine ***[28]****.* Brown solid, 76% yield, mp 177–178 °C; IR (ATR) ν (cm^{-1}) 1518, 1405, 1317, 1231, 777, 692, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, J=4.9, 1.2 Hz, 1H), 7.20–7.30 (m, 4H), 7.42–7.48 (m, 1H), 7.49–7.56 (m, 2H), 7.60–7.68 (m, 2H), 8.03 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 107.2, 116.6, 118.2, 123.7, 126.7, 127.6, 128.0, 128.1, 128.4, 128.7, 129.0, 133.7, 143.3, 143.8. HRMS (EI) m/z calcd for $C_{17}H_{11}BrN_2S$ $[M]^+$: 354.9905, found: 354.9885.

3.7. Procedure for Suzuki cross-coupling reaction of 6-bromo-3-substituted imidazo[1,2-*a*]pyridines under microwave irradiation

To a solution of 6-bromo-3-substituted imidazo[1,2-*a*]pyridine (0.26 mmol) dissolved in 2 mL of DMF in a vial microwave tube with a stir bar, boronic acid (0.31 mmol), potassium carbonate (0.52 mmol), triphenylphosphine (0.052 mmol) and palladium(II) acetate (0.026 mmol) were added under argon. The reaction vessel was sealed with a silicon septum and subjected to microwave irradiation for 20 min at 140 °C. The reaction mixture was then allowed to cool to room temperature, diluted with dichloromethane (15 mL) and extracted (3×). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The crude material obtained was purified by column chromatography on silica gel (EtOAc/PE) to give polysubstituted imidazo[1,2-*a*]pyridine derivatives **29** to **31**.

3.7.1. 6-(4-Methoxyphenyl)-3-(3-methoxyphenyl)-2-phenylimidazo [1,2-a]pyridine ***[29]****.* White solid, 93% yield, mp 139 °C; IR (ATR) ν (cm^{-1}) 2925, 1606, 1480, 1275, 1235, 1024, 770, 696. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 3.90 (s, 3H), 6.89 (dd, J=8.2, 1.8 Hz, 1H), 7.01 (s, 1H), 7.05–7.07 (m, 3H), 7.23–7.30 (m, 3H), 7.34 (d, J=7.9 Hz, 1H), 7.39 (d, J=8.6 Hz, 2H), 7.45 (dd, J=9.2, 1.5 Hz, 1H), 7.69–7.71 (m, 2H), 7.73 (d, J=9.7 Hz, 1H), 8.05 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.4 (OCH3), 55.4 (OCH3), 112.7 (CH), 113.2 (CH), 115.2, 117.3, 119.5, 120.7, 121.4, 121.7, 125.4, 126.7, 127.5, 128.0, 128.4, 130.2, 132.2, 132.2, 134.2, 139.1, 142.7, 144.0, 160.1, 160.2. HRMS (EI) m/z calcd for $C_{27}H_{22}N_2O_2$ $[M]^+$: 407.1760, found: 407.1742.

3.7.2. 6-(4-Methoxyphenyl)-2-phenyl-3-(4-trifluoromethylphenyl) imidazo[1,2-a]pyridine ***[30]****.* White solid, 92% yield, mp 173 °C; IR (ATR) ν (cm^{-1}) 1499, 1493, 1324, 1245, 1115, 1064, 814, 695. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.94 (d, J=8.7 Hz, 2H), 7.32–7.32 (m, 3H), 7.39 (d, J=8.7 Hz, 2H), 7.43–7.49 (m, 1H), 7.55–7.64 (m, 4H), 7.73 (d, J=9.3 Hz, 1H), 7.77 (d, J=8.1 Hz, 2H), 8.05 (d, J=0.6 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 114.6, 117.6, 119.5, 119.8, 122.7, 125.4, 126.2, 126.7 (CH), 127.2, 128.0, 128.1, 128.3, 128.5, 129.7, 130.6, 131.0, 133.7, 133.8, 143.9, 144.5, 159.7. HRMS (EI) m/z calcd for $C_{27}H_{19}F_3N_2O$ $[M+H]^+$: 445.1528, found: 445.1533.

3.7.3. 6-(4-Methoxyphenyl)-3-(3-methoxyprop-1-ynyl)-2-phenylimidazo[1,2-a]pyridine ***[31]****.* Brown oil, 86% yield; IR (ATR) ν

(cm^{-1}) 2928, 2360, 1499, 1060, 814. ^1H NMR (400 MHz, $CDCl_3$) δ 3.53 (s, 3H), 3.87 (s, 3H), 4.57 (s, 2H), 7.03 (d, J=8.7 Hz, 2H), 7.36–7.41 (m, 1H), 7.45–7.52 (m, 3H), 7.53 (d, J=8.7 Hz, 2H), 7.69 (dd, J=9.2, 0.8 Hz, 1H), 8.27–8.34 (m, 2H), 8.39 (dd, J=1.7, 0.8 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 57.9, 60.9, 75.8, 97.8, 104.4, 114.7, 117.3, 121.8, 127.2, 127.3, 127.4, 128.3, 128.6, 128.7, 129.6, 133.4, 144.5, 149.0, 159.8. HRMS (EI) m/z calcd for $C_{24}H_{20}N_2O_2$ $[M+H]^+$: 369.1603, found: 369.1586.

3.8. Procedure for Sonogashira cross-coupling reaction under microwave irradiation

To a solution of imidazo[1,2-*a*]pyridine **2** or **15** (0.29 mmol) in 2 mL of a mixture of a mixture of DMF/Et_3N (1/1, v/v) in a vial microwave tube, alkyne (0.38 mmol), copper iodide (0.058 mmol) and bis(triphenylphosphine)palladium dichloride (0.014 mmol) were added under argon. The reaction vessel was sealed with a silicon septum and subjected to microwave irradiation for 20 min at 140 °C. The reaction vessel was cooled to room temperature, diluted with dichloromethane (15 mL) and extracted (3×). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The crude material was purified by column chromatography on silica gel (EtOAc/PE) to give polysubstituted imidazo[1,2-*a*]pyridine derivatives **32** and **33**.

*3.8.1. 4-[6-(3-Methoxyprop-1-ynyl)-2-phenylimidazo[1,2-a]pyridin-3-yl]-2-methylbut-3-yn-2-ol [**32**].* Yellow solid, 91% yield, mp 106 °C; IR (ATR) ν (cm^{-1}) 3226, 2985, 2361, 1498, 1098, 808. ^1H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 6H), 3.47 (s, 1H), 3.49 (s, 3H), 4.35 (s, 2H), 7.20 (dd, J=9.2, 1.6 Hz, 1H), 7.30–7.35 (m, 3H), 7.56 (dd, J=9.2, 1.6 Hz, 1H), 8.15 (s, 1H), 8.16–8.22 (m, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.5, 58.0, 60.4, 65.9, 70.8, 82.4, 87.1, 106.9, 109.2, 117.0, 127.1, 128.0, 128.5, 128.8, 129.1, 132.8, 143.8, 148.4. HRMS (EI) m/z calcd for $C_{22}H_{20}N_2O_2$ $[M+H]^+$: 345.1603, found: 345.1584.

*3.8.2. 3-(3-Methoxyprop-1-ynyl)-2-phenyl-6-phenylethynylimidazo[1,2-a]pyridine [**33**].* Brown oil, 90% yield; IR (ATR) ν (cm^{-1}) 2925, 2306, 1494, 1092, 888. ^1H NMR (400 MHz, $CDCl_3$) δ 3.53 (s, 3H), 4.57 (s, 2H), 7.35–7.40 (m, 5H), 7.45–7.48 (m, 2H), 7.53–7.57 (m, 2H), 7.60 (dd, J=9.2, 0.8 Hz, 1H), 8.25–8.31 (m, 2H), 8.46–8.51 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 58.0, 60.8, 75.2, 85.4, 91.4, 98.2, 104.3, 110.1, 117.2, 122.6, 127.3, 127.8, 128.6, 128.7, 128.9, 128.9, 129.4, 131.7, 133.1, 144.1, 149.2. HRMS (EI) m/z calcd for $C_{25}H_{18}N_2O$ $[M+H]^+$: 363.1479, found: 363.1497.

3.9. Procedure for the one-pot double dissimilarly Sonogashira cross-coupling reaction under microwave irradiation

To a argon degassed solution of 3,6-dihalogenoimidazo[1,2-*a*]pyridines **1** or **14** (100 mg 0.250 mmol) in 2 mL of a mixture of DMF/Et_3N (1/1, v/v) in a vial microwave tube were subsequently added alkyne **I** (0.275 mmol), copper iodide (0.050 mmol) and bis(triphenylphosphine)palladium dichloride (0.012 mmol). The reaction vessel was sealed with a silicon septum and subjected to microwave irradiation for 10 min at 70 °C. Upon cooling to room temperature alkyne **II** (0.375 mmol) was injected into the tube via a syringe and the reaction mixture was subjected again to microwave irradiation at 140 °C for 45 min. The reaction was cooled to room temperature, quenched with water (15 mL), and extracted with dichloromethane (2×15 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (EtOAc/PE) to give polysubstituted imidazo[1,2-*a*]pyridine derivatives **34**–**38**.

*3.9.1. 3-[2-Phenyl-6-(phenylethynyl)imidazo[1,2-a]pyridin-3-yl]-prop-2-yn-1-ol [**34**].* Yellow solid, 70% yield, mp 162 °C; IR (ATR) ν (cm^{-1}) 3242, 1595, 1494, 1029, 808. ^1H NMR (400 MHz, $CDCl_3$) δ 3.98 (s, 1H), 4.65 (s, 2H), 7.28 (dd, J=9.2, 1.6 Hz, 1H), 7.30–7.34 (m, 1H), 7.35 (d, J=7.4 Hz, 1H), 7.36–7.38 (m, 4H), 7.52–7.54 (m, 2H), 7.57 (dd, J=9.2, 0.7 Hz, 1H), 8.12–8.16 (m, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 51.7, 73.9, 85.3, 91.5, 100.9, 104.4, 110.1, 116.7, 122.6, 127.0, 127.6, 128.6, 128.6, 128.8, 128.9, 129.5, 131.7, 132.6, 143.9, 148.4. HRMS (EI) m/z calcd for $C_{24}H_{16}N_2O$ $[M+H]^+$: 349.1341, found: 349.1323.

*3.9.2. 2-Methyl-4-[2-phenyl-6-(phenylethynyl)imidazo[1,2-a]pyridin-3-yl]but-3-yn-2-ol [**35**].* Yellow solid, 55% yield, mp 141 °C; IR (ATR) ν (cm^{-1}) 3257, 2980, 1498, 1391, 1314, 756, 687. ^1H NMR (400 MHz, $CDCl_3$) δ 1.73 (s, 6H), 3.20–3.40 (m, 1H), 7.32 (dd, J=9.2, 1.6 Hz, 1H), 7.33–7.36 (m, 1H), 7.37–7.43 (m, 5H), 7.55–7.59 (m, 2H), 7.61 (dd, J=9.2, 0.8 Hz, 1H), 8.20–8.23 (m, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.5, 65.9, 71.0, 85.4, 91.4, 104.4, 106.8, 110.0, 117.0, 122.6, 127.2, 127.5, 128.5, 128.6, 128.8, 128.9, 129.2, 131.7, 132.9, 143.8, 148.4. HRMS (EI) m/z calcd for $C_{20}H_{20}N_2O$ $[M+H]^+$: 377.1654, found: 377.1646.

*3.9.3. 4-[3-(3-Hydroxyprop-1-ynyl)-2-phenylimidazo[1,2-a]-pyridin-6-yl]-2-methylbut-3-yn-2-ol [**36**].* Yellow solid, 68% yield, mp 187 °C; IR (ATR) ν (cm^{-1}) 3247, 2980, 1498, 1395, 1023, 703. ^1H NMR (400 MHz, DMSO-d_6) δ 0.89 (s, 6H), 3.63 (s, 2H), 6.57–6.63 (m, 2H), 6.63–6.70 (m, 2H), 6.74–6.79 (m, 1H), 7.36–7.42 (m, 2H), 7.69 (s, 1H). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 31.5, 51.1, 66.4, 70.7, 81.1, 91.4, 106.0, 108.7, 111.5, 117.4, 128.2, 129.1, 129.6, 130.1, 131.1, 133.8, 145.1, 148.1. HRMS (EI) m/z calcd for $C_{21}H_{18}N_2O_2$ $[M+H]^+$: 331.1447, found: 331.1431.

*3.9.4. 3-(2-Phenyl-3-(phenylethynyl)imidazo[1,2-a]pyridin-6-yl)-prop-2-yn-1-ol [**37**].* Yellow solid, 75% yield, mp 169 °C; IR (ATR) ν (cm^{-1}) 3249, 2923, 2200, 1498, 1025, 748, 687. ^1H NMR (400 MHz, $CDCl_3$) δ 2.60–2.87 (m, 1H), 4.50 (s, 2H), 7.22 (dd, J=9.2, 1.5 Hz, 1H), 7.37–7.43 (m, 4H), 7.46–7.50 (m, 2H), 7.57–7.63 (m, 3H), 8.32–8.37 (m, 2H), 8.41 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 51.5, 77.6, 81.7, 89.6, 101.9, 105.1, 109.3, 117.2, 122.5, 127.4, 128.2, 128.7, 128.7, 128.9, 129.1, 129.2, 131.5, 133.1, 144.1, 148.6. HRMS (EI) m/z calcd for $C_{24}H_{16}N_2O$ $[M+H]^+$: 349.1341, found: 349.1330.

*3.9.5. 2-Methyl-4-[2-phenyl-3-(phenylethynyl)imidazo[1,2-a]pyridin-6-yl]-but-3-yn-2-ol [**38**].* Yellow solid, 74% yield, mp 170 °C; IR (ATR) ν (cm^{-1}) 3241, 2924, 1497, 1396, 1162, 750, 686. ^1H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 6H), 7.19 (dd, J=9.2, 1.5 Hz, 1H), 7.36–7.42 (m, 5H), 7.45–7.49 (m, 2H), 7.58–7.62 (m, 3H), 8.34–8.36 (m, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.5, 65.6, 77.7, 78.2, 96.1, 101.8, 105.0, 109.5, 117.1, 122.5, 127.4, 127.9, 128.7, 128.9, 129.0, 129.3, 131.5, 133.1, 144.0, 148.6. HRMS (EI) m/z calcd for $C_{26}H_{20}N_2O$ $[M+H]^+$: 377.1642, found: 377.1600.

3.10. Procedure for the one-pot double dissimilarly Suzuki cross-coupling under microwave irradiation

To a argon degassed solution of 3-bromo-6-iodoimidazo[1,2-*a*]pyridine **1** (100 mg 0.250 mmol) in DMF (2 mL) in a vial microwave tube were subsequently added Ar–$B(OH)_2$ **I** (0.275 mmol), potassium carbonate (0.501 mmol), triphenylphosphine (0.050 mmol) and palladium(II) acetate (0.025 mmol). The reaction vessel was sealed with a silicon septum and subjected to microwave irradiation for 30 min at 120 °C with stirring. Upon cooling to room temperature Ar–$B(OH)_2$ **II** (0.375 mmol) was added into the tube and the reaction mixture was subjected again to microwave irradiation at 140 °C for 2 h. The reaction vessel was cooled to room temperature, quenched with water (15 mL), and extracted with dichloromethane (2×15 mL). The combined organic layers were

dried over magnesium sulfate, filtered, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (EtOAc/PE) to afford polysubstituted imidazo[1,2-*a*]pyridine derivatives **30**, **39** and **40**.

*3.10.1. 4-[6-(4-Methoxyphenyl)-2-phenylimidazo[1,2-a]pyridi-ne-3-yl]-benzaldehyde [**39**].* Yellow solid, 71% yield, mp 204 °C; IR (ATR) ν (cm^{-1}) 2720, 1697, 1602, 1498, 1388, 1244, 1176, 1020, 813, 773. ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 6.97 (d, J=8.7 Hz, 2H), 7.27–7.34 (m, 3H), 7.42 (d, J=8.7 Hz, 2H), 7.48 (dd, J=9.3, 1.6 Hz, 1H), 7.58–7.62 (m, 2H), 7.68 (d, J=8.1 Hz, 2H), 7.75 (d, J=9.2 Hz, 1H), 8.03 (d, J=8.1 Hz, 2H), 8.14 (s, 1H), 10.10 (s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 114.7, 117.7, 119.6, 120.1, 126.2, 127.2, 128.0, 128.1, 128.5, 128.5, 129.7, 130.8, 131.1, 133.8, 136.1, 136.3, 144.3, 144.7, 159.7, 191.5. HRMS (EI) m/z calcd for $C_{27}H_{20}N_2O_2$ $[M+H]^+$: 405.1603, found: 405.1586.

*3.10.2. 6-(4-Methoxyphenyl)-2-phenyl-3-thiophen-3-yl-imida-zo[1,2-a]pyridine [**40**].* White solid, 71% yield, mp 135 °C; IR (ATR) ν (cm^{-1}) 2920, 1608, 1496, 1247, 1115, 1035, 773. ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 6.95 (d, J=8.7 Hz, 2H), 7.18 (dd, J=4.9, 1.2 Hz, 1H), 7.24–7.29 (m, 1H), 7.29–7.35 (m, 2H), 7.42 (d, J=8.7 Hz, 2H), 7.44 (s, 1H), 7.49 (dd, J=2.9, 1.2 Hz, 1H), 7.55 (dd, J=4.9, 2.9 Hz, 1H), 7.69–7.72 (m, 3H), 8.07–8.09 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.5, 114.6, 116.5, 117.3, 120.2, 125.5, 126.3, 126.7, 127.3, 127.6, 128.0, 128.1, 128.4, 128.9, 129.7, 130.0, 134.3, 143.5, 144.2, 159.6. HRMS (EI) m/z calcd for $C_{24}H_{18}N_2OS$ $[M+H]^+$: 383.1218, found: 383.1201.

References and notes

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