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Synthesis of Luminescent Fused Imidazole Bicyclic Acetic Esters by a Multicomponent Palladium Iodide-Catalyzed Oxidative Alkoxycarbonylation Approach

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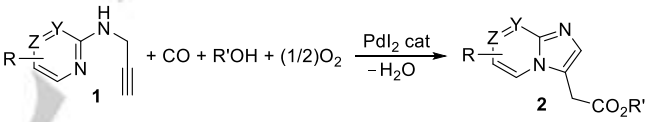
Abstract: A new multicomponent catalytic approach to important fused imidazole bicyclic acetic esters, whose core is present in many biologically active principles, is presented. It is based on the sequential cyclization-alkoxycarbonylation-isomerization of readily available *N*-heterocyclic propargylamine derivatives, carried out under oxidative conditions using a simple catalytic system consisting of PdI_2 (1 mol%) in conjunction with KI (1 equiv), in the presence of AcONa as additive (1 equiv) at 100 °C under 20 bar of a 4:1 mixture CO-air. Under the optimized conditions, several *N*-(prop-2-yn-1-yl)pyridin-2-amines were smoothly converted into alkyl 2-(imidazo[1,2-*a*]pyridin-3-yl)acetates in fair yields (51-77%). The method was also applied to the conversion of *N*-(prop-2-yn-1-yl)pyrimidin-2-amine into 2-(imidazo[1,2-*a*]pyrimidin-3-yl)acetate and of *N*-(prop-2-yn-1-yl)pyrazin-2-amine into 2-(imidazo[1,2-*a*]pyrazin-3-yl)acetate. Some of the newly synthesized bicyclic derivatives have shown promising luminescence properties.

Introduction

The development of novel catalytic approaches based on multicomponent alkoxycarbonylation reactions is one of the most attractive modern methods for the synthesis of high value added molecules containing the ester function.[1] Of particular interest are those methods that are based on sequential heterocyclization-alkoxycarbonylation of suitably functionalized alkynes, which may lead to heterocyclic esters in one step starting from readily available starting materials.[2] In this field, our research group has contributed many examples,[3] by employing a very simple catalytic system based on PdI_2 in conjunction with KI, as reviewed in our recently published account.[1f]

In this paper, we report the application of our PdI_2/KI-catalyzed oxidative carbonylation methodology [1f, 3] to the realization of a novel synthesis of fused imidazole bicyclic acetic esters **2**,[4-6] starting from readily available *N*-heterocyclic propargylamine derivatives **1**, as shown in Scheme 1. This multicomponent carbonylative approach allows obtaining in one step bicyclic scaffolds of particular interest, which are known to possess important biological activities.[7-9] We have also found that some of the newly synthesized bicyclic derivatives show important luminescence properties, characterized by high fluorescence quantum yield and emission centred in the visible region.



(Y,Z = CH, N; R = H, Me, Cl, Br, NO_2; R' = alkyl)

Scheme 1. Synthesis of fused imidazole bicyclic acetic esters **2** by multicomponent palladium iodide-catalyzed oxidative alkoxycarbonylation of *N*-heterocyclic propargylamine derivatives **1**.

Results and Discussion

Oxidative cyclization-alkoxycarbonylation leading to imidazole bicyclic acetic esters

Starting materials *N*-heterocyclic propargylamine derivatives **1** were easily prepared by *N*-propargylation of *N*-Boc-2-aminopyridines, *N*-Boc-2-aminopyrimidine, or *N*-Boc-2-aminopyrazine, followed by deprotection, as detailed in the Experimental Section.

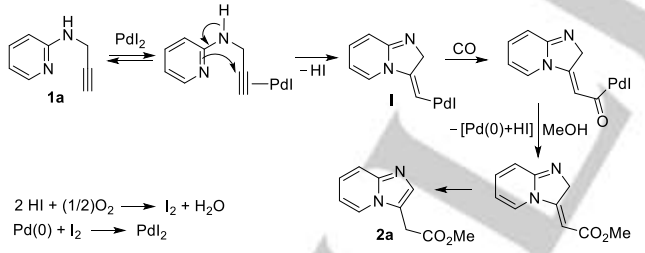
The initial oxidative carbonylation experiments were carried out using *N*-(prop-2-yn-1-yl)pyridin-2-amine **1a** as model substrate. By allowing to react **1a** with CO (16 bar), O_2 (from air, 4 bar), and MeOH (also used as solvent; 0.2 mmol of **1a** per mL of MeOH) at 100 °C in the presence of 1 mol% of PdI_2 and 1 equiv of KI, after 1 h methyl 2-(imidazo[1,2-*a*]pyridin-3-yl)acetate **2a** was obtained in 43% isolated yield at total **1a** conversion (the formation of chromatographically immobile materials accounted for the rest of the converted substrate) (Table 1, entry 1).

Table 1. PdI_2/KI-catalyzed oxidative methoxycarbonylation of *N*-(prop-2-yn-1-yl)pyridin-2-amine **1a** to 2-(imidazo[1,2-*a*]pyridin-3-yl)acetate **2a** under different conditions.[a]

Entry	KI [equiv]	Base [equiv]	Concentration of **1a**[b]	*T* [°C]	P_{CO}:P_{air} [bar][c]	Yield of **2a** [%][d]
1	1	none	0.2	100	16:4	43
2	1	none	0.2	80	16:4	35
3	1	none	0.1	100	16:4	37
4	1	none	0.4	100	16:4	31
5	0.5	none	0.2	100	16:4	38
6	1	none	0.2	100	32:8	40
7	1	AcONa [1]	0.2	100	16:4	65
8	1	MeONa [1]	0.2	100	16:4	50

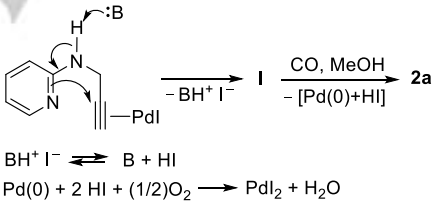
[a] Unless otherwise noted, all reactions were carried out in MeOH at 100 °C for 1 h in the presence of 1 mol% of PdI_2. Substrate conversion was quantitative. Formation of unidentified heavy products (chromatographically immobile materials) accounted for the difference between substrate conversion and product yield. [b] Mmol of **1a** per mL of MeOH. [c] At 25 °C. [d] Isolated yield based on starting **1a**.

This encouraging initial result indicated that the nitrogen of the pyridinic ring of **1a**, assisted by conjugation with the exocyclic nitrogen, was sufficiently nucleophilic to attack the triple bond coordinated to Pd(II), to give the vinylpalladium intermediate **I** after an *anti* 5-*exo*-*dig*–type dearomative heterocyclization (Scheme 2; anionic iodide ligands are omitted for clarity). This complex would then undergo carbon monoxide insertion, nucleophilic displacement by MeOH, and rearomatization to give the final product and Pd(0). The latter is then reoxidized to PdI_2 according to the mechanism we already demonstrated[1f,10] involving oxidation of HI to I_2 followed by oxidative addition of I_2 to Pd(0) (Scheme 2).



Scheme 2. Proposed mechanism for the PdI_2/KI-catalyzed oxidative alkoxycarbonylation of *N*-(prop-2-yn-1-yl)pyridin-2-amine **1a** to give 2-(imidazo[1,2-*a*]pyridin-3-yl)acetate **2a**.

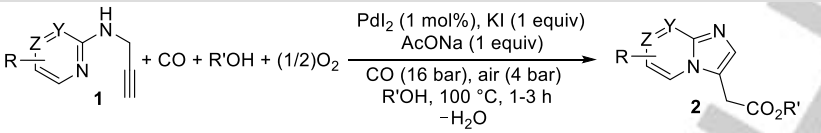
To increase the yield toward **2a**, we next carried out a brief optimization study, by varying some typical reaction parameters (such as temperature, **1a** concentration, KI amount,[11] and total pressure); however, no improvement could be achieved, as shown in Table 1, entries 2-6. Nevertheless, it was possible to raise the yield of **2a** up to 65% by performing the initial reaction in the presence of 1 equiv of AcONa (Table 1, entry 7). This effect is probably due to a partial deprotonation of the substrate amino group, which makes the pyridine conjugated nitrogen more nucleophilic, thus facilitating the heterocyclization against other possible substrate degradation pathways (Scheme 3). The use of more basic sodium methoxide instead of sodium acetate did not give any further improvement (Table 1, entry 8), probably because a stronger base tended to hinder Pd(0) reoxidation by efficiently "sequestering" the HI necessary for its reconversion to catalytically active PdI_2 (Scheme 3).

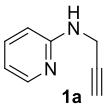
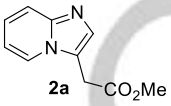
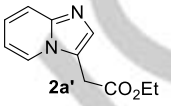
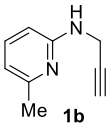
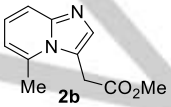
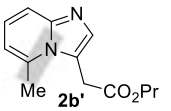
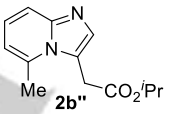
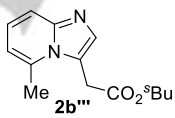
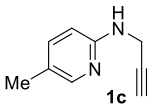
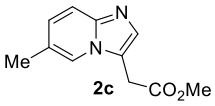
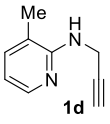
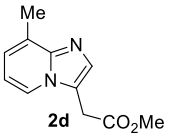
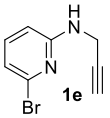
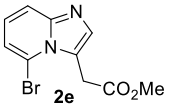
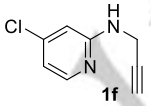
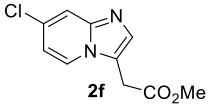
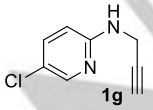
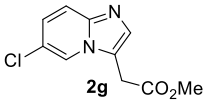
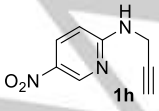
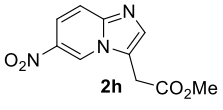
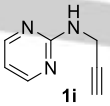
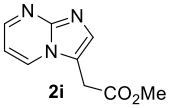


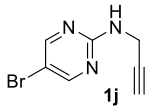
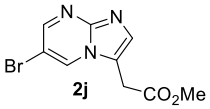
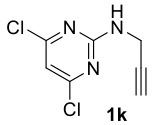
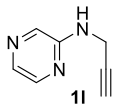
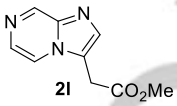
Scheme 3. Possible effects of an external base (B) on the reaction mechanism.

The method was then applied to the use of other alcohols and differently substituted *N*-(prop-2-yn-1-yl)pyridin-2-amines, using the conditions optimized for **1a**, and the results are shown in Table 2. As can be seen from the Table, the reaction of **1a** with EtOH led to the corresponding ethyl ester **2a'** in a yield similar (63%, Table 2, entry 2) to that obtained in MeOH (65%, Table 2, entry 1) after the same reaction time (1 h). The presence of a methyl group at C-6, as in **1b**, led to slightly better results in terms of product yields, in MeOH (72%, Table 2, entry 3, to be compared with entry 1) as well as in higher alcohols (70-75%, Table 2, entries 4-6; with more sterically hindered secondary alcohols reaction time was increased to 3 h). A methyl group at C-5 did not affect the yield significantly (57% of **2c**, Table 2, entry 7), while a slight decrease was observed when the methyl group was present at C-3, probably owing to the steric effect exerted on nitrogen deprotonation (yield of **2d** = 51%, Table 2, entry 8). Interestingly, fair to good yields of methyl 2-(imidazo[1,2-*a*]pyridin-3-yl)acetates **2e-h** (60-77%) were obtained when the pyridine ring was substituted with an halogen or a nitro group in different positions (Table 2, entries 9-12).

Table 2. Synthesis of fused imidazole bicyclic acetic esters **2** by multicomponent PdI_2-catalyzed oxidative alkoxycarbonylation of *N*-heterocyclic propargylamine derivatives **1**.[a]



Entry	**1**	R'	Time [h]	**2**	Yield of **2a** [%][d]
1	 **1a**	Me	1	 **2a**	65
2	**1a**	Et	1	 **2a'**	63
3	 **1b**	Me	1	 **2b**	72
4	**1b**	Pr	1	 **2b'**	78
5	**1b**	*i*-Pr	3	 **2b''**	75
6	**1b**	*sec*-Bu	3	 **2b'''**	70
7	 **1c**	Me	1	 **2c**	57
8	 **1d**	Me	1	 **2d**	51
9	 **1e**	Me	1	 **2e**	72
10	 **1f**	Me	1	 **2f**	66
11	 **1g**	Me	1	 **2g**	77
12	 **1h**	Me	1	 **2h**	60
13	 **1i**	Me	3	 **2i**	58

14	 **1j**	Me	3	 **2j**	40[c]
15	 **1k**	Me	3		0[d]
16	 **1l**	Me	6	 **2l**	70

[a] Unless otherwise noted, all reactions were carried out in R'OH (0.2 mmol of **1** per mmol of solvent) at 100 °C under 20 bar (at 25 °C) of a 4:1 mixture of CO-air, in the presence of PdI_2 (1 mol%), KI (1 equiv), and AcONa (1 equiv). Substrate conversion was quantitative in all cases. Formation of unidentified heavy products (chromatographically immobile materials) accounted for the difference between substrate conversion and product yield. [b] Isolated yield based on starting **1**. [c] The reaction also led to the formation of dimethyl 2-(((5-bromopyrimidin-2-yl)amino)methyl)maleate **3j** (from oxidative *syn* double alkoxycarbonylation of the triple bond [1f, 9]) in 20% isolated yield. [d] The reaction led to the formation of dimethyl 2-(((4,6-dichloropyrimidin-2-yl)amino)methyl)maleate **3k** in 40% isolated yield.

To further assess the synthetic potentiality of our method, we then tested the reactivity of substrates bearing an additional nitrogen on the ring. The reaction of *N*-(prop-2-yn-1-yl)pyrimidin-2-amine **1i** was slower with respect to the same reaction of **1a**, and was accordingly carried out for 3 h. In any case, it afforded the desired 2-(imidazo[1,2-*a*]pyrimidin-3-yl)acetate **2i** with an acceptable isolated yield (58%, Table 2, entry 13). However, in the presence of a bromine substituent at C-5 the carbonylation process was less selective, and led to the formation of dimethyl 2-(((5-bromopyrimidin-2-yl)amino)methyl)maleate **3j** (from oxidative *syn* double alkoxycarbonylation of the triple bond)[1f,10] in 20% yield in addition to the expected methyl 2-(6-bromoimidazo[1,2-*a*]pyrimidin-3-yl)acetate **2j** (40% yield, Table 2, entry 14). Moreover, unfortunately, the presence of two chlorine substituents at C-4 and C-6, as in **1k**, completely inhibited the formation of the imidazopyrazinacetate and led to the formation of dimethyl 2-(((4,6-dichloropyrimidin-2-yl)amino)methyl)maleate **3k** in 40% yield, besides unidentified products deriving from substrate decomposition (Table 2, entry 15). This is propably due to the strong electron-withdrawing effect exerted by the two chlorine atoms, which significantly lowers nitrogen nucleophilicity, thus causing the competing triple bond dicarbonylation to become the main reaction pathway. On the other hand, carbonylation of *N*-(prop-2-yn-1-yl)pyrazin-2-amine **1l** turned out to be successful, as the corresponding 2-(imidazo[1,2-*a*]pyrazin-3-yl)acetate **2l** could be isolated in 61% yield (Table 2, entry 16).

Fluorescence emission properties of imidazole bicyclic acetic esters and quantum yield measurements

Considering the extensive conjugation of the newly synthesized imidazole bicyclic acetic esters, we have studied the luminescence properties of some representative products.

Figure 1 shows the quantitative absorption spectra of **2a**, **2b**, **2e**, **2i**, **2j**, and **2l** registered in $CHCl_3$. The main effect that can be inferred from the analysis of Fig. 1 is the pronounced bathochromic shift of the absorption spectrum observed in imidazopyrimidinyl acetates **2i** and **2j**, with respect to the imidazopyridinyl acetates **2a-e** and imidazopyrazinyl acetate **2l**. Moreover, a bromine substituent at C-6 in **2j** led to a significant enhancement of the molar absorption coefficient value with respect to **2i**. Within the imidazopyridinyl series, a red shift of the absorption was observed in bromine-containing **2e** with respect to **2a**.

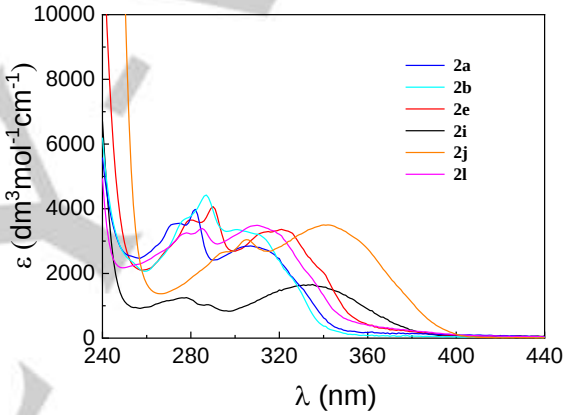


Figure 1. Quantitative absorption spectra of **2a**, **2b**, **2e**, **2i**, **2j** and **2l** in $CHCl_3$.

The normalized fluorescence emission spectra of the same compounds in $CHCl_3$ are shown in Figure 2. As already found in the absorption measurements, also in the emission spectra the molecules bearing a Br substituent and/or having an imidazopyrimidinyl structure, namely **2e**, **2i** and **2j**, exhibit large bathochromic shifts with respect to the other compounds. If one takes into account the parent molecule, **2a**, it is possible to rationalize the effect of substitution and changes in the molecular skeleton on the emission properties. Introduction of an electron-donating methyl group at C-5 in the imidazopyridinyl series, as in **2b**, induces a modest blue shift (8 nm) of the emission spectra, while, as already pointed out, the presence of an electron-withdrawing Br substituent at the same position, as in **2e**, results in the pronounced red shift effect (83 nm). Moving from the imidazopyridinyl core (**2a**) to the imidazopyrimidinyl one (**2i** and **2j**), a significant red shift (52 nm and 63 nm, respectively) of the emission spectrum is observed. On the other hand, **2l**, bearing an imidazopyrazinyl nucleus, produces only a little bathochromic shift (4 nm).

For all the six molecules investigated, the corresponding emission maxima and the fluorescence quantum yields were also measured and collected in Table 3.

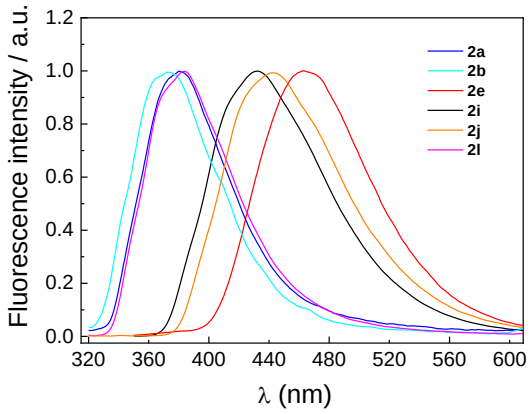


Figure 2. Normalized emission spectra of **2a**, **2b**, **2e**, **2i**, **2j**, and **2l** in $CHCl_3$.

Table 3. Fluorescence emission maxima (λ_{max}) and fluorescence quantum yields for compounds **2a**, **2b**, **2e**, **2i**, **2j**, and **2l** measured upon UV excitation at 340 nm, in $CHCl_3$.

Compound	λ_{max} [nm]	ϕ_F
2a	380	0.020
2b	372	0.013
2e	463	0.090
2i	432	0.600
2j	443	0.210
2k	384	0.090

The same analysis carried out for the emission spectra can be performed for the quantum yield values as well. With respect to the parent molecule, substitution at C-5 with an electron-donating Me group leads to a decrease of the emission quantum yield from 0.02 (**2a**) to 0.013 (**2b**). On the other hand, the introduction at the same position of the electron-withdrawing Br atom causes an enhancement of the quantum yield to 0.09 (**2e**). A more remarkable increase in the emission quantum yield is also observed upon replacement of the imidazopyridinyl core of **2a** (ϕ_F = 0.02) with the imidazopyrazinyl one (**2l**, ϕ_F = 0.09) and even more with the imidazopyrimidinyl nucleus, where the largest values are found: ϕ_F = 0.21 and 0.60 for **2j** and **2i**, respectively. The latter two molecules, along with **2e**, considering both their uncommon high fluorescence quantum yields and important emission centred in the visible region, are certainly of notable interest, especially for biological and biomedical applications.

Conclusion

In conclusion, we have found that it is possible to convert readily available *N*-(prop-2-yn-1-yl)pyridin-2-amines into high valued added alkyl 2-(imidazo[1,2-*a*]pyridin-3-yl)acetates by a catalytic, multicomponent oxidative carbonylative approach, based on the use of a very simple catalytic system (PdI_2–KI) with the simplest external oxidant possible (O_2 from air). The method could be successfully applied to a variety of *N*-(prop-2-yn-1-yl)pyridin-2-amines bearing substituents on the pyridine ring with different electronic characteristics, and using MeOH, primary as well as secondary alcohols as external nucleophiles. The method also worked nicely for the conversion of *N*-(prop-2-yn-1-yl)pyrimidin-2-amine and 2-(imidazo[1,2-*a*]pyrimidin-3-yl)acetate into the corresponding fused imidazole bicyclic acetic esters. In some cases, however, limitations were observed, for example the reaction was not selective when the pyrimidine presented electron-withdrawing groups, as it preferentially led to triple bond oxidative dialkoxycarbonylation.

Some of the bicyclic compounds synthesized in this work were also tested for their luminescence properties. In particular, two compounds within those tested (that are, **2i** and **2j**) showed a very interesting fluorescence emission, centred in the visible region associated with remarkably high quantum yields (0.60 and 0.21, respectively), which make them excellent candidates for biomedical applications.

Experimental Section

General Experimental Methods. Melting points are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$, DMSO-d_6 or CD_3OD at 300 MHz and 75 MHz, respectively, with Me_4Si as internal standard. Chemical shifts (δ) and coupling constants (*J*) are given in ppm and in Hz, respectively. IR spectra were taken with an FT-IR spectrometer. All reactions were analyzed by TLC on silica gel 60 F_{254} and by GC-MS analysis using a GC–MS apparatus at 70 eV ionization voltage equipped with a 95% methyl polysiloxane - 5% phenyl polysiloxane capillary columns (30 m × 0.25 mm, 0.25 μm). Column chromatography was performed on silica gel 60 (70–230 mesh). Evaporation refers to the removal of solvent under reduced pressure. The HRMS spectra were taken on Q-TOF-MS mass spectrometer, equipped with an electrospray ion source (ESI) operated in dual ion mode. 10 μL of the sample solutions (CH_3OH) were introduced by continuous infusion at a flow rate of 200 L min^{-1} with the aid of a syringe pump. Experimental conditions were performed as follows: capillary voltage, 4000 V; nebulizer pressure, 20 psi; flow rate of drying gas, 10 L/min; temperature of sheath gas, 325 °C; flow rate of sheath gas, 10 L/min; skimmer voltage, 60 V; OCT1 RF Vpp, 750 V; fragmentor voltage, 170 V. The spectra data were recorded in the *m/z* range of 100– 1000 Da in a centroid pattern of full-scan MS analysis mode. The MS/MS data of the selected compounds were obtained by regulating diverse collision energy (18–45 eV).

For both UV-vis absorption and emission measurements, $CHCl_3$ Spectronorm grade (99.2%), purchased from VWR Chemicals, was used as received. Absorption spectra were recorded on a Perkin-Elmer Lambda 800 UV-vis absorption double-beam spectrophotometer. Fluorescence emission spectra were recorded on a Jobin Yvon Floromax-4 spectrofluorometer, equipped with a system for spectral correction; the quantum yields were determined by using quinine sulphate in 1N H_2SO_4 (quantum yield ϕ_F = 0.546)[12] as the standard. The corrected areas of the sample and the standard emissions were compared and their values introduced in the following equation, which accounts for the differences in absorbance and refraction index of the sample (A_F, n_F) and standard (A_{St}, n_{St}) solutions:

$$\phi_F = \phi_{St} \frac{(Area)_F}{(Area)_{St}} \frac{A_{St}}{A_F} \frac{n_F^2}{n_{St}^2}$$

Sample concentrations were always adjusted to keep the absorbance below 0.1 to have a linear relation between the emitted intensity and the absorbance and avoid self-absorption phenomena. The error in the ϕ_F values is estimated to be below 10%.

Substrates **1a-b**, **1g** ,**1l** and **1i** were prepared according a known procedure starting from corresponding 2-aminopyridine.[6a] Substrate **1k** was prepared according a known procedure starting from 2,4,6-trichloropyrimidine.[13] Substrate **1c-f**, **1h** and **1j** were prepared as described below. All other materials were commercially available and were used without further purification.

General Procedure for the Preparation of *N*-(prop-2-yn-1-yl)pyridin-2-amines 1c-f and 1h

To a cooled (0°C) solution of Boc protected *N*-(prop-2-yn-1-yl)pyridin-2-amine[14] (6.10 mmol) [*N*-Boc-5-methyl-*N*-(prop-2-yn-1-yl)pyridin-2-amine, 1.50 g; *N*-Boc-3-methyl-*N*-(prop-2-yn-1-yl)pyridin-2-amine, 1. 50 g; *N*-Boc-6-bromo-*N*-(prop-2-yn-1-yl)pyridin-2-amine, 1.90 g; *N*-Boc-4-chloro-*N*-(prop-2-yn-1-yl)pyridin-2-amine, 1.63 g; *N*-Boc-5-nitro-*N*-(prop-2-yn-1-yl)pyridin-2-amine, 1.69 g] in anhydrous CH_2Cl_2 (6 mL), was added, under nitrogen, trifluoroacetic acid (6 mL, 78.4 mmol). To the mixture was then added a 3 M NaOH solution (26 mL) and then Et_2O (10 mL). The organic layer was separated, washed with water and brine, and then was dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude product was purified by flash column chromatography on silica gel using 8:2 hexane-AcOEt as eluent.

*5-Methyl-N-(prop-2-yn-1-yl)pyridin-2-amine (**1c**).* Yield: 803 mg, starting from 1.50 g of *N*-Boc-5-methyl-*N*-(prop-2-yn-1-yl)pyridin-2-amine (90%). Yellow solid, mp: 53-55°C; IR (KBr): ν = 1620 (m), 1505 (s), 1381 (m), 1296 (m), 1142 (w), 1088 (w), 1026 (m), 910 (w), 818 (s) cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.00-7.94 (m, 1 H, H-6), 7.28 (dd, *J* = 8.4, 2.3, 1 H, H-4), 6.43 (d, *J* = 8.4, 1 H, H-3), 4.78 (s, br, 1 H, NH), 4.09 (dist dd, *J* = 5.5, 2.2, 2 H, CH_2), 2.20 (t, *J* = 2.2, 1 H, ≡CH), 2.18 (s, 3 H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 147.7, 138.4, 122.7, 107.5, 81.4, 70.7, 31.9, 17.4; GC/MS (EI): *m/z* = 146 (M^+, 50), 145 (100), 131 (4), 118 (10), 93 (30); HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_9H_{10}N_2Na^+$ 169.0736; Found: 169.0740.

*3-Methyl-N-(prop-2-yn-1-yl)pyridin-2-amine (**1d**).* Yield: 740 mg, starting from 1.50 g of *N*-Boc-3-methyl-*N*-(prop-2-yn-1-yl)pyridin-2-amine (83%). Yellow solid, mp: 61-66°C; IR (KBr): ν = 3210 (m), 2099 (w), 1597 (m), 1504 (s), 1381 (m), 1327 (m), 1281 (m), 1180 (w), 1119 (m), 1072 (w), 995 (w), 910 (w), 787 (s) cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.07-8.01 (m, 1 H, H-6), 7.27-7.20 (m, 1 H, H-4), 6.58 (dd, *J* = 7.1, 5.1, 1 H, H-5), 4.32 (s, br, 1 H, NH), 4.28 (d, *J* = 2.3, 2 H, CH_2), 2.23 (t, *J* = 2.3, 1 H, ≡CH), 2.10 (s, 3 H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.7, 145.4, 137.0, 117.1, 113.7, 81.9, 70.7, 31.4, 16.8; GC/MS (EI): *m/z* = 146 (M^+, 90), 145 (100), 131 (4), 118 (7), 93 (10), 78 (3); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_9H_{10}N_2Na^+$ 169.0736; Found: 169.0732

*6-Bromo-N-(prop-2-yn-1-yl)pyridin-2-amine (**1e**).* Yield: 1.06 g, starting from of 1.90 g of *N*-Boc-6-bromo-*N*-(prop-2-yn-1-yl)pyridin-2-amine (82%). Colorless solid, mp: 98-99°C; IR (KBr): ν = 3279 (m), 1605 (s), 1558 (m), 1528 (w), 1443 (s), 1350 (w), 1273 (w), 1165 (w), 1088 (s), 972 (m), 764 (m) cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.35-7.25 (m, 1 H, H-4), 6.80 (d, *J* = 7.5, 1 H, H-3 or H-5), 6.42 (d, *J* = 8.2, 1 H, H-5 or H-3), 5.21 (s, br, 1 H, NH), 4.11 (dd, *J* = 5.9, 2.5, 2 H, CH_2), 2.25-2.21 (m, 1 H, ≡CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 140.2, 139.6, 116.9, 105.3, 80.1, 71.4, 31.8; GC/MS (EI): *m/z* = 212 [(M+2)$^+$, 11), 210 (M^+, 11), 131 (100), 104 (8), 92 (13), 78 (21); HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_8H_7BrN_2Na^+$ 232.9685; Found: 232.9677.

*4-Chloro-N-(prop-2-yn-1-yl)pyridin-2-amine (**1f**).* Yield: 823 mg, starting from 1.63 g of *N*-Boc-4-chloro-*N*-(prop-2-yn-1-yl)pyridin-2-amine (81%). Colorless solid, mp: 74-76°C; IR (KBr): ν = 3233 (m), 1605 (s), 1582 (s), 1528 (w), 1458 (m), 1265 (m), 1103 (w), 864 (w), 826 (w), 795 (m) cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 5.5, 1 H, H-6), 6.65 (dd, *J* = 5.5, 1.5, 1 H, H-5), 6.49 (d, *J* = 1.5, 1 H, H-3), 5.24 (s, br, 1 H, NH), 4.11 (dist dd, *J* = 5.5, 2.3, 2 H, CH_2), 2.25 (t, *J* = 2.3, 1 H, ≡CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.6, 149.0, 144.9, 114.3, 107.2, 80.4, 71.3, 31.7 ; GC/MS (EI): *m/z* = 167 [(M+2)$^+$, 36), 165 (M^+, 100), 138 (9), 113 (32), 78 (32); HRMS (ESI - TOF) *m/z*: [M + H]$^+$ Calcd for $C_8H_8ClN_2^+$ 167.0371; Found: 167.0368.

*5-Nitro-N-(prop-2-yn-1-yl)pyridin-2-amine (**1h**).* Yield: 594 mg, starting from 1.69 g of *N*-Boc-5-nitro-*N*-(prop-2-yn-1-yl)pyridin-2-amine (55%). Colorless solid, mp: 133-135°C; IR (KBr): ν = 3256 (m), 2126 (w), 1605 (s), 1493 (m), 1331 (m), 1296 (m), 1123 (m), 822 (w), 764 (w), 721 (w); ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 8.96 (d, *J* = 2.7, 1 H, H-6), 8.44 (t, br, *J* = 5.0, 1 H, NH), 8.23-8-14 (m, 1 H, H-4), 6.65 (dd, *J* = 9.4, 0.5, 1 H, H-3), 4.28-4.16 (m, 2 H, CH_2), 3.16 (t, *J* = 2.4, 1 H, ≡CH); ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 160.6, 146.4, 135.0, 132.2, 108.5 (br), 80.8, 73.3, 30.2; GC/MS (EI): *m/z* = 177 (M^+,17), 131 (100), 119 (5), 104 (9), 78 (26); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_8H_7N_3O_2Na^+$ 200.0430; Found: 200.0426.

Preparation of 5-Bromo-*N*-(prop-2-yn-1-yl)pyrimidin-2-amine 1j

A Schlenk flask was charged under nitrogen with 5-bromo-2-chlorpyrimidine (400 mg, 2.07 mmol), anhydrous CH_3CN (4.1 mL), propargylamine (240 mg, 4.31 mmol) and DIPEA (800 mg, 6.19 mmol). The reaction mixture was heated at 80°C and then allowed to stir at this temperature for 15 hours. The crude product was concentrated by rotary evaporation and then purified on silica using hexane-ethyl acetate (9:1) as eluent (yield: 358 mg, 82%). *5-Bromo-N-(prop-2-yn-1-yl)pyrimidin-2-amine **1j**.* Colorless solid, mp: 159 – 162°C; IR (KBr): ν = 3210 (m), 2122 (vw), 1605 (s), 1520 (m), 1435 (m), 1327 (w), 1103 (w), 787 (m) cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 8.44 (s, 1 H, aromatic), 7.83 (t, br, *J* = 5.9, 1 H, NH), 4.02 (dd, *J* = 5.9, 2.3, 2 H,CH_2), 3.03 (t, *J* = 2.3, 1 H, ≡CH); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 160.0, 158.0, 106.0, 81.6, 72.3, 30.3; GC/MS (EI): *m/z* = 213 [(M+2)$^+$, 88], 211 (M^+, 85), 186 (16), 160 (44), 158 (45), 132 (100), 105 (32), 79 (67); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ calcd for $C_7H_6BrN_3Na^+$ 233.9637; Found: 233.9624

General Procedure for the Oxidative Carbonylation of *N*-Heterocyclic Propargylamine derivatives 1 to Give 2a-j, 2l, and 3j,k (Table 2)

A 35 mL T316 stainless steel autoclave was charged in the presence of air with PdI_2 (3.5 mg, 9.72×10^{-3} mmol), KI (161 mg, 0.972 mmol), anhydrous R'OH (4.9 mL), substrate **1** (0.97 mmol) (**1a**, 128 mg; **1b**, 142 mg; **1c**, 142 mg; **1d**, 142 mg; **1e**, 205 mg; **1f**, 162 mg; **1g**, 162 mg; **1h**, 172 mg, **1i**, 129 mg; **1j**, 206 mg; **1k**, 196 mg; **1l**, 129 mg) and AcONa (80 mg; 0.97 mmol). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (16 bar) and air (up to 20 bar). After being stirred at 100 °C for 1-6 h, the autoclave was cooled, degassed and opened. After evaporation of the solvent, products **2a-j**, **2l**, and **3j,k** were purified by column chromatography on silica gel using 99:1 $CHCl_3$-MeOH as eluent.

*Methyl 2-(imidazo[1,2-a]pyridin-3-yl)acetate (**2a**).* Yield: 120 mg, starting from 128 mg of **1a** (65%). Colorless solid, mp: 99-101°C, lit.[15] 110 – 113°C ; IR (KBr): ν = 1736 (s), 1501 (m), 1435 (w), 1343 (m), 1292 (m), 1182 (s), 995 (w), 895 (w), 760 (s) cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD): δ = 8.24 (d, br, *J* = 6.9, 1 H, H-5), 7.58-7.49 (m, 1 H, H-8), 7.49 (s, 1 H, H-2), 7.35–7.24 (m, 1 H, H-7), 6.94 (td, *J* = 6.9, 1.0, 1 H, H-6), 4.09 (s, 2 H, CH_2), 3.71 (s, 3 H, CO_2CH_3); ^{13}C NMR (75 MHz, CD_3OD): δ = 171.5, 146.9, 132.8, 126.4, 125.8, 119.5, 117.6, 113.7, 52.8, 30.0; GC/MS (EI): *m/z* = 190 (M^+, 15), 131 (100), 78 (23); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{10}H_{10}N_2O_2Na^+$ 213.0634; Found: 213.0635.

*Ethyl 2-(imidazo[1,2-a]pyridin-3-yl)acetate (**2a'**).* Yield: 125 mg, starting from 128 mg of **1a** (63%). Yellow oil; IR (film): v = 1732 (s), 1682 (w), 1636 (w), 1501 (m), 1312 (m), 1180 (m), 1026 (m), 752 (s) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 8.34-8.27 (m, 1 H, H-5), 7.61-7.53 (m, 1 H, H-8), 7.49 (s, 1 H, H-2), 7.28-7.21 (m, 1 H, H-7), 6.97-6.90 (t, *J* = 6.7, 1 H, H-6), 4.14 (s, 2 H, C*H*$_2$CO$_2$Et), 4.11 (q, *J* = 7.1, 3 H, OCH$_2$), 1.20 (t, *J* = 7.1, 3 H, Me); ^{13}C NMR (75 MHz, DMSO–d_6): δ = 169.3, 144.8, 132.6, 124.8, 123.8, 117.7, 116.8, 111.6, 60.6, 29.0, 13.9; GC/MS (EI): *m/z* = 204 (M^+, 13), 131 (100), 78 (16); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{11}H_{12}N_2O_2Na^+$ 227.0791; Found: 227.0791.

*Methyl 2-(5-methylimidazo[1,2-a]pyridin-3-yl)acetate (**2b**).* Yield: 143 mg, starting from 142 mg of **1b** (72%). Yellow oil. IR (Film): v = 1736 (s), 1639 (w), 1535 (w), 1512 (m), 1439 (m), 1292 (m), 1200 (m), 1173 (m), 1150 (m), 1002 (m), 783 (m) cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ = 7.40 (s, 1 H, H-2), 7.36 (d, *J* = 9.0, 1 H, H-8), 7.12 (dd, *J* = 9.0, 6.9, 1 H, H-7), 6.59 (d, *J* = 6.9, 1 H, H-6), 4.25 (s, 2 H, CH$_2$), 3.70 (s, 3 H, CO$_2$CH$_3$), 2.72 (s, 3 H, CH$_3$ at C-5); ^{13}C NMR (75 MHz, CD_3OD): δ = 173.4, 148.9, 137.9, 135.2, 126.8, 120.5, 115.9, 115.0, 53.0, 33.1, 19.7; GC/MS (EI): *m/z* = 204 (M^+, 13), 145 (100), 92 (9); HRMS (ESI - TOF) m/z: [M + Na]$^+$ Calcd for $C_{11}H_{12}N_2O_2Na^+$ 227.0791; Found: 227.0790.

*Propyl 2-(5-methylimidazo[1,2-a]pyridin-3-yl)acetate (**2b'**).* Yield: 176 mg, starting from 142 mg of **1b** (78%). Yellow oil; IR (film): v = 1732 (s), 1643 (w), 1539 (w), 1504 (w), 1454 (m), 1292 (m), 1177 (m), 1057 (w), 775 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.49-7.39 (m, 1 H, H-8), 7.45 (s, 1 H, H-2), 7.04-6.94 (m, 1 H, H-7), 6.44 (d, br, *J* = 6.6, 1 H, H-6), 4.13 (s, 2 H, CH$_2$CO), 4.06 (t, *J* = 7.1, 2 H, OC*H*$_2$), 2.73 (s, 3 H, Me at C-5), 1.62 (hexuplet, *J* = 7.1, 2 H, C*H*$_2$CH$_3$), 0.87 (t, *J* = 7.1, 3 H, CH$_2$C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 147.9, 135.7, 135.4, 124.3, 118.2, 116.1, 113.5, 66.9, 32.9, 21.8, 19.9, 10.3; GC/MS (EI): *m/z* = 232 (M^+, 15), 145 (100), 117 (2), 92 (6); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{13}H_{16}N_2O_2Na^+$ 255.1104; Found: 255.1105.

*Isopropyl 2-(5-methylimidazo[1,2-a]pyridin-3-yl)acetate (**2b"**).* Yield: 169 mg, starting from 142 mg of **1b** (75%). Yellow solid, mp: 80 – 85°C; IR (KBr): v = 1721 (s), 1636 (w), 1535 (w), 1512 (m), 1373 (w), 1288 (m), 1204 (s), 1150 (m), 1111 (m), 941 (w), 779 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.51-7.43 (m, 1 H, H-8), 7.47 (s, 1 H, H-2), 7.04 (dd, *J* = 9.0, 6.8, 1 H, H-7), 6.53-6.46 (m, 1 H, H-6), 5.04 (heptuplet, *J* = 6.3, 1 H, OC*H*Me$_2$), 4.12 (s, 2 H, CH$_2$), 2.78 (s, 3 H, Me at C-5), 1.23 [d, *J* = 6.3, 6 H, CH(C*H*$_3$)$_2$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 148.0, 135.6, 135.5, 124.3, 118.3, 116.4, 113.5, 69.0, 33.4, 21.7, 20.0; GC/MS (EI): *m/z* = 232 (M^+, 18), 145 (100), 92 (8); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{13}H_{16}N_2O_2Na^+$ 255.1104; Found: 255.1099.

*sec-Butyl 2-(5-methylimidazo[1,2-a]pyridin-3-yl)acetate (**2b"'**).* Yield: 167 mg, starting from 142 mg of **1b** (70%). Yellow oil; IR (film): v = 1728 (s), 1643 (w), 1535 (w), 1512 (m), 1288 (m), 1180 (m), 995 (w), 880 (w), 779 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.52-7.41 (m, 1 H, H-8), 7.45 (s, 1 H, H-2), 7.03 (dd, *J* = 8.9, 6.8, 1 H, H-7), 6.49 (d, br, *J* = 6.8, 1 H, H-6), 4.87 (hexuplet, *J* = 6.3, 1 H, OC*H*CH$_2$), 4.13 (s, 2 H, CH$_2$CO), 2.77 (s, 3 H , Me at C-5), 1.66-1.43 (m, 2 H, C*H*$_2$CH$_3$), 1.20 (d, *J* = 6.3, 3 H, CHC*H*$_3$), 0.83 (t, *J*= 7.4, 3 H, CH$_2$C*H*$_3$). ^{13}C NMR (75 MHz, CDCl3): δ = 170.5, 135.7, 135.4, 124.4, 118.4, 116.3, 113.6, 73.6, 33.3, 28.6, 20.0, 19.3, 9.5; GC/MS (EI): *m/z* = 246 (M^+, 16), 145 (100), 92 (7); HRMS (ESI - TOF) *m/z*: [M + H]$^+$ Calcd for $C_{14}H_{19}N_2O_2^+$ 247.1441; Found: 247.1448.

*Methyl 2-(6-methylimidazo[1,2-a]pyridin-3-yl)acetate (**2c**).* Yield: 113 mg, starting from 142 mg of **1c** (57%). Yellow solid, mp: 86 – 88°C, lit. [13] 90 – 93°C; IR (KBr): 1732 (s), 1651 (w), 1512 (m), 1454 (m), 1315 (m), 1169 (m), 999 (w), 802 (w) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 8.14 (s, 1 H, H-5), 7.55-7.38 (m, 2 H, H-2 + H-8), 7.17-7.06 (m, 1 H, H-7), 4.12 (s, 2 H, CH$_2$), 3.65 (s, 3 H, CO$_2$CH$_3$), 2.30 (s, 3 H, CH$_3$ at C-6); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.8, 143.7, 132.3, 126.9, 122.2, 120.9, 117.2, 116.2, 51.9, 28.8, 17.6 .6; GC/MS (EI): *m/z* = 204 (M^+, 20), 145 (100), 92 (11); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{11}H_{12}N_2O_2Na^+$ 227.0791; Found: 227.0784.

Methyl 2-(8-methylimidazo[1,2-a]pyridin-3-yl)acetate (***2d***). Yield: 101 mg, starting from 142 mg of **1d** (51%). Yellow oil; IR (film): 1728 (s), 1636 (w), 1489 (m), 1435 (m), 1312 (m), 1258 (m), 1173 (s), 995 (w), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 6.8, 1 H, H-5), 7.54 (s, 1 H, H-2), 7.00 (dt, *J* = 6.8, 1.1, 1 H, H-7), 6.78 (t, *J* = 6.8, 1 H, H-6), 3.94 (s, 2 H, CH$_2$), 3.71 (s, 3 H, CO$_2$CH$_3$), 2.62 (s, br, 3 H, Me at C-8); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.6, 146.4, 132.5, 127.8, 122.9, 121.4, 117.0, 112.5, 52.4, 30.3, 17.0; GC/MS (EI): *m/z* = 204 (M^+, 19), 145 (100), 92 (7); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{11}H_{12}N_2O_2Na^+$ 227.0791; Found: 227.0790.

*Methyl 2-(5-bromoimidazo[1,2-a]pyridin-3-yl)acetate (**2e**).*Yield: 188 mg, starting from 205 mg of **1e** (72%). Yellow solid, mp: 109-112°C; IR (KBr): v = 1736 (s), 1628 (m), 1458 (w), 1435 (w), 1281 (m), 1204 (m), 1173 (m), 1150 (m), 995 (w), 779 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.66-7.55 (m, 1 H, H-7), 7.52 (s, br, 1 H, H-2), 7.05-6.95 (m, 2 H, H-6 + H-7), 4.30 (s, 2 H, CH$_2$), 3.74 (s, 3 H, CO$_2$CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 148.3, 136.1, 124.6, 120.2, 118.5, 117.5, 113.2, 52.5, 33.3; GC/MS (EI): *m/z* = 270 [(M+ 2)$^+$, 26], 268 (M^+, 28), 211 (92), 209 (100), 130 (17); HRMS (ESI - TOF) m/z: [M + Na]$^+$ Calcd for $C_{10}H_9BrN_2O_2Na^+$ 290.9740; Found: 290.9740.

*Methyl 2-(7-chloroimidazo[1,2-a]pyridin-3-yl)acetate (**2f**).* Yield: 144 mg, starting from 162 mg of **1f** (66%). Yellow solid, mp: 122-125°C; IR (KBr): v = 1736 (s), 1628 (m), 1489 (m), 1404 (w), 1319 (m), 1204 (m), 1173 (m), 1065 (m), 980 (w), 895 (w), 856 (w), 802 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 7.3, 0.7, 1 H, H-5), 7.62 (dist dd, *J* = 2.0, 0.7, 1 H, H-8), 7.53 (s, 1 H, H-2), 6.84 (dd, *J* = 7.3, 2.0, 1 H, H-6), 3.93 (s, 2 H, CH$_2$), 3.72 (s, 3 H, CO$_2$CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 145.8, 134.1, 130.8, 124.0, 117.1, 116.8, 114.0 52.6, 30.1; GC/MS (EI): *m/z* = 226 [(M+ 2)$^+$, 8], 224 (M^+, 25), 167 (35), 165 (100), 112 (18), 102 (3), 76 (9); HRMS (ESI - TOF) m/z: [M + Na]$^+$ Calcd for $C_{10}H_9ClN_2O_2Na^+$ 247.0245; Found: 247.0248.

*Methyl 2-(6-chloroimidazo[1,2-a]pyridin-3-yl)acetate (**2g**).* Yield: 168 mg, starting from 162 mg of **1g** (77%). Colorless solid, mp: 116 - 118°C; IR (KBr): v = 1721 (s), 1597 (s), 1539 (m), 1439 (m), 1289 (s), 1223 (m), 1103 (m), 1018 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.13-8.05 (m, 1 H, H-5), 7.64-7.51 (m, 2 H, H-2 + H-8), 7.16 (dd, *J* = 9.6, 1.9, 1 H, H-7), 3.94 (s, 2 H, CH$_2$), 3.74 (s, 3 H, CO$_2$CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 144.4, 134.2, 125.5, 121.6, 120.8, 118.3, 117.4, 52.6, 30.0; GC/MS (EI): *m/z* = 226 [(M+2)$^+$, 8], 224 (M^+, 23), 167 (34), 165 (100), 114 (7), 112 (22); HRMS (ESI - TOF) *m/z*: [M + H]$^+$ Calcd for $C_{10}H_{10}ClN_2O_2^+$ 225.0425; Found: 225.0431.

*Methyl 2-(6-nitroimidazo[1,2-a]pyridin-3-yl)acetate (**2h**).* Yield: 137 mg, starting from 172 mg of **1h** (60%). Colorless solid, mp: 152-155 °C; IR (KBr): v = 1728(s), 1643 (m), 1551 (m), 1504 (m), 1342 (m), 1304 (s), 1211 (m), 1111 (m), 903 (w), 725 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 9.27-9.21 (m, 1 H, H-5), 7.98 (dd, *J* = 9.9, 2.2, 1 H, H-7), 7.73 (s, 1 H, H-2), 7.70 (d, *J* = 9.9, 1 H, H-8), 4.08 (s, 2 H, CH$_2$), 3.77 (s, 3 H, CO$_2$CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9, 146.0, 137.3, 136.7, 124.4, 119.9, 118.2, 117.6, 52.8, 29.8; GC/MS = 235 (M^+, 27), 176 (100), 130 (73), 103 (30); HRMS (ESI - TOF) m/z: [M + Na]$^+$ Calcd for $C_{10}H_9N_3O_4Na^+$ 258.0485; Found: 258.0480.

*Methyl 2-(imidazo[1,2-a]pyrimidin-3-yl)acetate (**2i**).* Yield: 108 mg, starting from 129 mg of **1i** (58%). Colorless solid, mp: 114-118°C; IR (KBr): v = 1721 (s), 1620 (m), 1520 (w), 1497 (w), 1435 (w), 1204 (m), 1096 (s), 980 (w), 795 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.56 (dd, *J* = 4.1, 2.0, 1 H, H-5 or H-7), 8.48 (dd, *J* = 6.9, 2.0, 1 H, H-7 or H-5), 7.71 (s, 1 H, H-2), 6.94 (dd, *J* = 6.9, 4.1, 1 H, H-6), 3.98 (s, 2 H, CH$_2$), 3.72 (s, 3 H, CO$_2$CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 149.5, 149.0, 134.7, 131.9, 115.6, 108.6, 52.6, 30.0; GC/MS (EI): *m/z* = 191 (M^+, 21), 132 (100), 106 (6), 79 (17); HRMS (ESI - TOF) m/z: [M + Na]$^+$ Calcd for $C_9H_9N_3O_2Na^+$ 214.0587; Found: 214.0587.

*Methyl 2-(6-bromoimidazo[1,2-a]pyrimidin-3-yl)acetate (**2j**).* Yield: 105 mg, starting from 206 mg of **1j** (40%). Colorless solid, mp: 191-193°C; IR (KBr): v = 1728 (s), 1474 (m), 1397 (w), 1350 (w), 1204 (m), 1180 (m), 1142 (w), 903 (w), 756 (w) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 9.28 (d, *J* = 2.3, 1 H, H-5 or H-7), 8.61 (d, *J* = 2.3, 1 H, H-7 or H-5), 7.69 (s, 1 H, H-2), 4.19 (s, 2 H, CH_2), 3.66 (s, 3 H, CO_2CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.5, 149.4, 146.2, 134.7, 133.4, 117.5, 103.5, 52.0, 28.6; GC/MS (EI): *m/z* = 271 [$(M+2)^+$, 28], 269 (M^+, 28), 212 (100), 210 (92), 159 (13), 157 (13), 131 (21); HRMS (ESI - TOF) m/z: $[M + Na]^+$ Calcd for $C_9H_8BrN_3O_2Na^+$ 291.9692; Found: 291.9692.

*Methyl 2-(imidazo[1,2-a]pyrazin-3-yl)acetate (**2l**). Yie*ld: 130 mg, starting from 129 mg of **1l** (70%). Yellow solid, mp: 117-120°C; IR (KBr): v = 1736 (s), 1489 (m), 1435 (w), 1350 (m), 1304 (m), 1204 (m), 1172 (m), 1026 (w), 895 (m), 818 (w), 772 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.11 (s, 1 H, H-8), 8.09-8.00 (m, 1 H, H-5 or H-6), 7.94 (d, *J* = 4.6, 1 H, H-6 or H-5), 7.74 (s, 1 H, H at C-2), 4.01 (s, 2 H, CH_2), 3.75 (s, 3 H, CO_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8, 144.0, 141.3, 135.4, 129.5, 118.4, 116.9, 52.7, 29.7; GC/MS (EI): *m/z* = 191 (M^+, 22), 132 (100), 79 (12); HRMS (ESI - TOF) m/z: $[M + H]^+$ Calcd for $C_9H_{10}N_3O_2^+$ 192.0768; Found: 192.0768.

*Dimethyl 2-(((5-bromopyrimidin-2-yl)amino)methyl)maleate (**3j**).* Yield: 64 mg, starting from 206 mg of **1j** (20%). Yellow oil; IR (KBr): v = 1728 (s), 1659 (w), 1574 (m), 1520 (m), 1435 (m), 1381 (m), 1265 (m), 1203 (m), 1173 (m), 1026 (w), 756 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.31 (s, 2 H, aromatic), 6.28 (t, *J* = 6.3, 1 H, NH), 6.10 (s, br, 1 H, =CH), 4.34 (dd, *J* = 6.3, 1.2, 2 H, CH_2), 3.82 (s, 3 H, CO_2Me), 3.73 (s, 3 H, CO_2Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.4, 165.5, 160.1, 158.4, 144.8, 121.5, 107.5, 52.6, 52.1, 43.5; GC/MS (EI): *m/z* = 331 [$(M^+ +2)^+$, 9], 329 [$(M)^+$, 8], 299 (23), 297 (25), 272 (100), 270 (91), 240 (40), 238 (35), 213 (30), 212 (46), 211 (32), 210 (40), 186 (25), 159 (20), 132 (15), 107 (20), 79 (30), 59 (66); HRMS (ESI - TOF) m/z: [M + Na]+ Calcd for $C_{11}H_{12}BrN_3O_4Na^+$ 351,9903; Found: 351.9897.

*Dimethyl 2-(((4,6-dichloropyrimidin-2-yl)amino)methyl)maleate (**3k**).* Yield: 124 mg, starting from 196 mg of **1k** (40%). Colorless solid, mp: 129-133°C; IR (KBr): v = 1721 (s), 1605 (m), 1558 (m), 1519 (m), 1435 (m), 1319 (m), 1257 (m), 1203 (m), 1165 (m), 1018 (w), 817 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ = 6.68 (s, 1 H, aromatic), 6.44 (t, br, *J* = 6.1, 1 H, NH), 6.13 (s, br, 1 H, =CH), 4.43-4.32 (m, 2 H, CH_2), 3.83 (s, 3 H, CO_2Me), 3.75 (s, 3 H, CO_2Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1, 165.4, 161.3, 143.3, 122.7, 110.2, 52.7, 52.2, 43.3; GC/MS (EI): *m/z* = 321 [$(M+2)^+$, 3], 319 (M^+, 4), 289 (36), 287 (61), 262 (62), 261 (66), 260 (100), 259 (83), 228 (38), 224 (48), 200 (30), 176 (37), 147 (21), 113 (25), 59 (44); HRMS (ESI - TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}Cl_2N_2O_4Na^+$ 342,0019; Found: 342.0021.

Keywords: bicyclic heterocycles • carbonylation • luminescent compounds • multicomponent reaction • palladium

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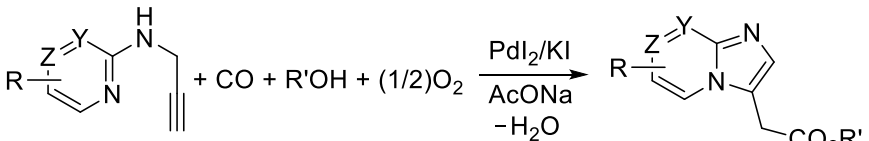

(R = H, Me, Cl, Br, NO_2; Y, Z = CH, N; R' = alkyl)

New luminescent bicyclic heterocycles have been synthesized in one step from readily available *N*-heterocyclic propargylamine derivatives by a palladium-catalyzed multicomponent carbonylation process, carried out under oxidative conditions using PdI_2 in conjunction with KI as the catalytic system, AcONa as base, and oxygen (from air) as external oxidant.