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Photoarylation of Pyridines using Aryldiazonium Salts and Visible Light: An EDA Approach

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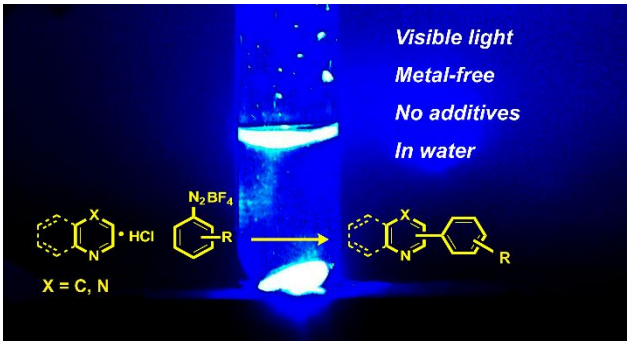
Graphical Abstract



Abstract

A metal-free methodology for the photoarylation of pyridines, in water, is described giving 2 and 4-arylated-pyridines in yields up to 96%. The scope of the aryldiazonium salts is presented showing important results depending on the nature and position of the substituent group in the diazonium salt, i.e., electron-donating or electron-withdrawing in the *ortho*, *meta* or *para* positions. Further heteroaromatics were also successfully photoarylated. Mechanistic studies and comparison between our methodology and similar metal-catalyzed procedures are presented, suggesting the occurrence of a visible light EDA complex which generates the aryl radical with no need for additional photocatalyst.

Introduction

Pyridine moieties are common in natural products, agrochemicals,[1-3] and drugs approved by the FDA.[4,5] Moreover, relevant clinical drugs such as Crizotinib, Enasidenib, Vismodegib, Nilotinib, Etoricoxib, Atazanavir, and Nevirapine, contain the pyridine nucleus directly linked/fused to aryl or heteroaryl units (Figure 1).[4-8] Therefore, the development of new and efficient methodologies for the direct C–H arylation or heteroarylation of this electron-deficient heterocycle is of great interest.

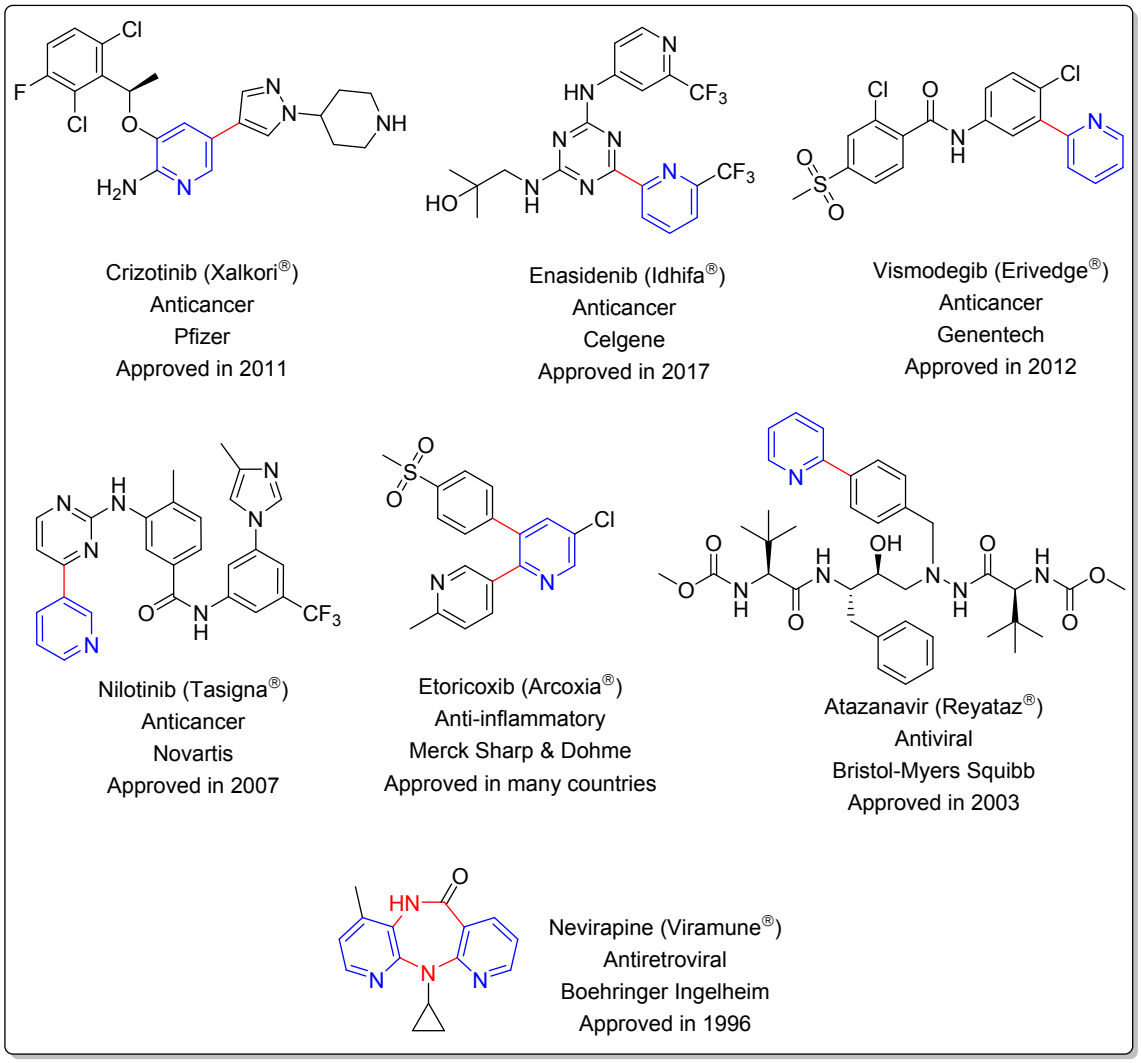
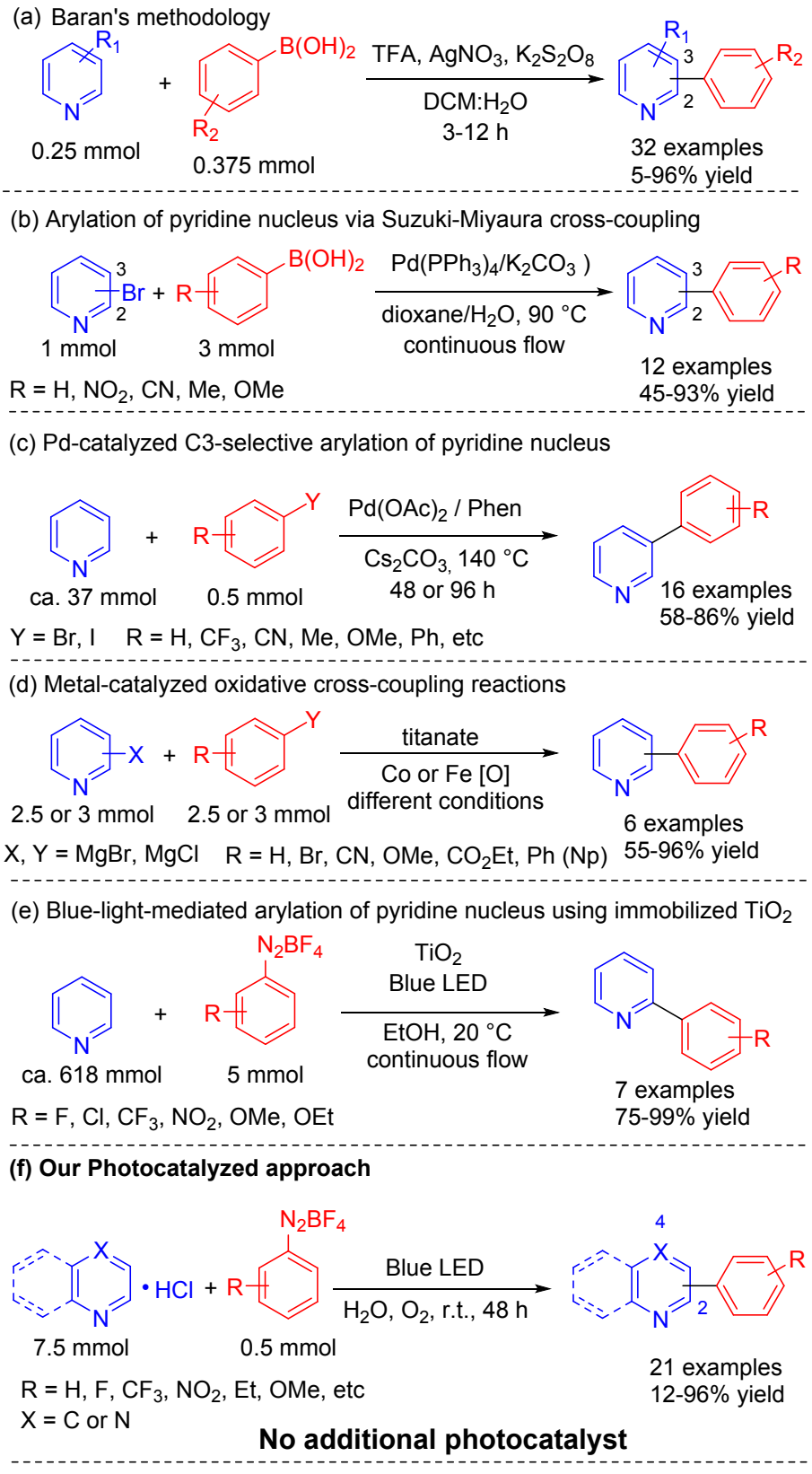


Figure 1. Structures of drugs which contain the pyridine nucleus (in blue).

The synthesis of biaryls containing a pyridine motif can be efficiently carried out by Baran's methodology (Scheme 1, Eq a),[9] in which silver nitrate and potassium persulfate are used for aryl-radical generation from boronic acids, and subsequent arylation of a variety of *N*-heterocycles. Classical cross-coupling reactions such as Suzuki-Miyaura,[10-14] Negishi,[15-17] Stille,[13,18,19] Hiyama,[20,21] and Kumada[22,23] have been developed (Scheme 1, Eq. b) and proved to be similarly efficient. These structures can also be synthesized by C–H activation reactions (Scheme 1, Eq. c),[24-26] oxidative cross-coupling reactions (Scheme 1, Eq. d),[27-29] and alternatively by radical-based methodologies,[30,31] which have received much attention recently in studies involving photocatalysis.[32-39] Such photocatalyzed reactions have been performed with various aryl radical precursors such as aryldiazonium[40-49] and diaryliodonium salts,[50,51] aryl carboxylic acids,[52] benzenesulfonyl chlorides (not tested with a pyridine nucleus),[53] arylazosulfones (tested with the pyrazolopyridine nucleus),[54,55] diazoanhydrides (with pyridine *N*-oxide),[56] and halo(hetero)arenes[57-59] in the presence of ruthenium complexes,[41,43,44,51] iridium complexes,[50,52,57] organic dyes,[47-49,58,59] metal oxides,[40,42,46] and other (photo)catalysts (Scheme 1, Eq. e).[60,61] However, the radical arylation of arenes and heteroarenes has been achieved with only a few aryl radical precursors, even in the absence of a photocatalyst.[50,55,56,62]



Scheme 1. Selected approaches for the synthesis of biaryls with one pyridine nucleus.

In 2017, Heinrich and co-workers[45] reported that the arylation of some arenes and heteroarenes with *p*-substituted aryl diazonium salts does not require the use of an additional photocatalyst and other additives, and can be conducted under simple UV-photocatalysis (250W, iron lamp, black glass filter), UV-Vis (250W, iron lamp, no filter) or visible-light (10W, blue LED lamp) irradiation using an argon or air atmosphere. They postulated that these arylations can be achieved by simple photoinduced radical generation from a CT complex, but no further mechanistic insights were reported. They also have shown the direct C–H arylation of 3-hydroxypyridine with some aryldiazonium salts, in 50-62% yields. However, this methodology[45] does not work for the aryldiazonium salt bearing a *para*-methoxy group even when an electron-rich (hetero)arene was employed as substrate (<10% isolated yields).

We now report a protocol for the direct C–H arylation of the pyridine nucleus and other *N*-heteroarenes, in water, with several aryldiazonium tetrafluoroborates substituted by electron-donor, -neutral and -acceptor groups and with no base or additives, at room temperature, and using visible-light irradiation (blue-LED) in the absence of photocatalysts (Scheme 1, Eq. f). We postulate the occurrence of a visible light EDA for the aryl radical generation which is supported by UV-Vis and ^{1}H and ^{1}H-^{15}N NMR.

Results and discussion

We started our investigation with pyridine hydrochloride (**1a**) and 4-methoxybenzenediazonium tetrafluoroborate (**2a**) as the model substrates using a homemade batch photoreactor with blue or white 30W LEDs (see details of the photoreactor setup in the Supporting Information). First, the reaction between (**1a**) (7.5

mmol) and **2a** (0.5 mmol) in MeOH (1.5 mL) was tested at r.t., under an O_2 atmosphere and in the dark, but only traces of the *2-arylated*-regioisomer **3a** could be detected by GC-MS after 48 h (Table 1, entry 1). Subsequently, we performed the reaction in the same conditions but in the presence of blue light (blue LEDs) obtaining a mixture of 2-aryl/4-aryl substituted pyridines (**3a**) in 84% yield (Table 1, entry 2).

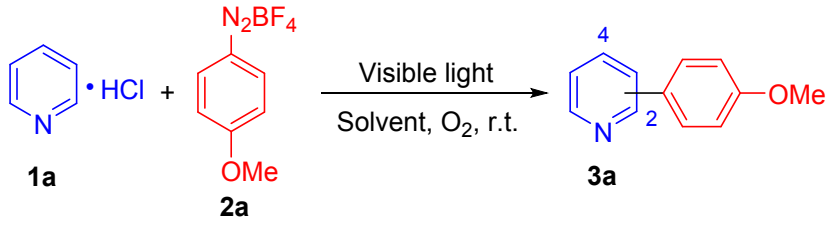
We also evaluated whether the activation of the pyridine moiety as the hydrochloride is needed, and carried out the same reaction with 7.5 mmol of free base pyridine and irradiation by blue LED resulting in a 20% yield of a mixture of the 2- and 4-*arylated*-regioisomers **3a** (Table 1, entry 3); this experiment allowed us to conclude that the use of pyridinium salts is essential in this protocol. Changing the amount of pyridine hydrochloride (**1a**) relative to the diazonium salt **2a** we found 41 to 90% yields of **3a** (Table 1, entries 4 and 5). Keeping 7.5 mmol of **1a** and increasing **2a** to 1 mmol also resulted in a lower yield (51%) (Table 1, entry 6) showing that high excesses of **1a** relative to **2a** are important for the efficiency of the protocol. Although the reaction with 10 mmol of **1a** significantly improved the yield of **3a** (Table 1, entry 5), we decided to continue the screening of conditions using 7.5 mmol of this substrate. It is important to highlight that this excess of pyridinium salt is necessary and will be clarified in the section of mechanistic studies.

The influence of the atmosphere, reaction time, and LED light source was also evaluated (Table 1, entries 7-9, respectively). It was observed that the yield of **3a** decreased when the reaction was performed under an argon atmosphere (75% yield, entry 7 *vs* 2) or when a shorter reaction time (24 h) was considered (72% yield, entry 8).

Additionally, when white LEDs were employed under the same reaction conditions (entry 9) a lower yield (59%) was obtained.

We also investigated the effect of other solvents (EtOH, DMF, DMSO and H_2O) or mixtures of solvents (DMF/MeOH, 1:1 or 1:2, v/v) on the yield of **3a** (Table 1, entries 10-15). To our delight, when H_2O was used as the solvent, the desired product **3a** was obtained in 96% yield under identical conditions (entry 15). It is worth noting that the yield of the arylated product **3a** increased with the increase in polarity of the solvent used in the reaction (Table 1, entries 11, 10, 2 and 15, respectively). The only exception was the reaction carried out in DMSO (entry 14). The robustness of the protocol (entry 16) was also tested reacting 2 mmols of **2a** in the same optimized conditions (entry 15), giving the product **3a** in 79% yield (0.3 g-scale). Finally, we checked the optimized reaction condition for the pyridine arylation (entry 15) in the absence of light, and again only traces of the *2-arylated*-regioisomer **3a** could be detected by GC-MS after 48 h (entry 17). These results showed that these arylation reactions are promoted by visible-light irradiation and do not require a photocatalyst to occur under mild and environmentally friendly conditions.

Table 1. Screening of the reaction conditions.[a]



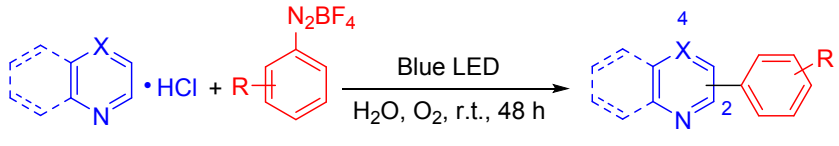
1a **2a** **3a**

Entry	1a (mmol)	2a (mmol)	Light source (30W)	Solvent	Time (h)	2-aryl:4-aryl[e]	Overall Yield 3a[f]
1	7.5	0.5	None	MeOH	48	-	Trace
2	7.5	0.5	Blue LED	MeOH	48	71:29	84
3	7.5[b]	0.5	Blue LED	MeOH	48	68:32	20
4	5	0.5	Blue LED	MeOH	48	67:33	41
5	10	0.5	Blue LED	MeOH	48	67:33	90
6	7.5	1	Blue LED	MeOH	48	68:32	55
7[c]	7.5	0.5	Blue LED	MeOH	48	71:29	75
8	7.5	0.5	Blue LED	MeOH	24	72:28	72
9	7.5	0.5	White LED	MeOH	48	73:27	59
10	7.5	0.5	Blue LED	EtOH	48	67:33	69
11	7.5	0.5	Blue LED	DMF	48	77:23	64
12	7.5	0.5	Blue LED	DMF/MeOH (1:1)	48	71:29	63
13	7.5	0.5	Blue LED	DMF/MeOH (1:2)	48	69:31	71
14	7.5	0.5	Blue LED	DMSO	48	73:27	82
15	7.5	0.5	Blue LED	H_2O	48	71:29	96
16[d]	30	2	Blue LED	H_2O	48	67:33	79
17	7.5	0.5	none	H_2O	48	-	Trace

[a] Reaction conditions: pyridine hydrochloride (**1a**) (5, 7.5 and 10 mmol), 4-methoxybenzenediazonium tetrafluoroborate (**2a**) (0.5 and 1 mmol) in solvent (1.5 mL) at r.t. under an O_2 atmosphere for 24 or 48 h. [b] With 7.5 mmol of free base pyridine. [c] Previously deoxygenated and maintained under argon

atmosphere. [d] scaled-up reaction performed in the same reaction conditions of entry 15, but in 6 mL of H_2O with **3a** obtained in 0.3 g-scale. [e] Determined after isolation. [f] Isolated yields

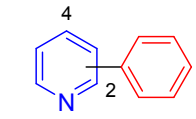
With the optimized reaction conditions in hands (Table 1, entry 15), we proceeded to evaluate the diazonium salt scope. As shown in Scheme 2, several aryldiazonium salts with different substitution patterns, substituted pyridines, quinoline and quinoxaline are compatible with our arylation protocol.



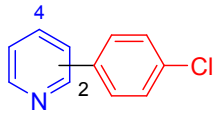
1a-g, X = C or N
7.5 mmol

2a-r
0.5 mmol

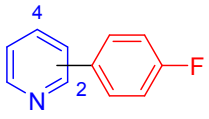
3b-x



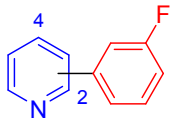
3b, 62%
2-aryl/4-aryl, 71:29



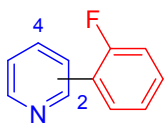
3c, 80%
2-aryl/4-aryl, 68:32



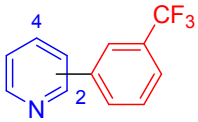
3d, 53%
2-aryl/4-aryl, 59:41



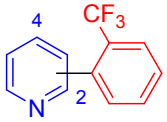
3e, 58%
2-aryl/4-aryl, 62:38



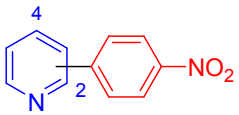
3f, 31%
2-aryl/4-aryl, 64:36



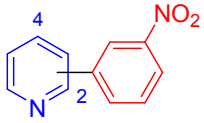
3g, 49%
2-aryl/4-aryl, 63:37



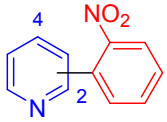
3h
2-aryl = 23%, 4-aryl = 0%



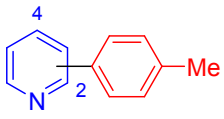
3i, 66%
2-aryl/4-aryl, 64:36



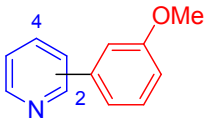
3j, 49%
2-aryl/4-aryl, 61:39



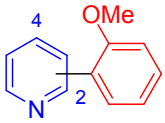
3k, 52%
2-aryl/4-aryl, 60:40



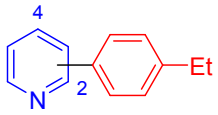
3l, 80%
2-aryl/4-aryl, 68:32



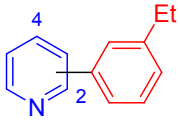
3m, 13%
2-aryl/4-aryl, 67:33



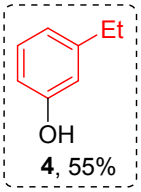
3n, 57%
2-aryl/4-aryl, 66:34



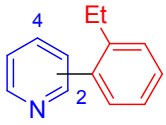
3o, 75%
2-aryl/4-aryl, 68:32



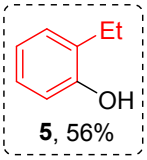
3p, 0%



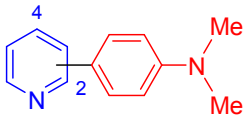
4, 55%



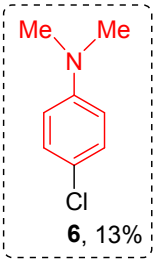
3q, 0%



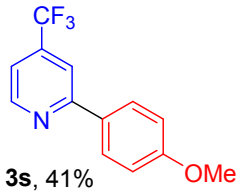
5, 56%



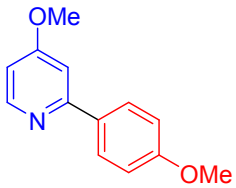
3r
2-aryl = 14%, 4-aryl = 0%



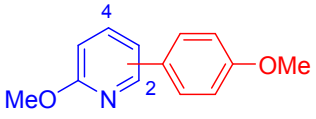
6, 13%



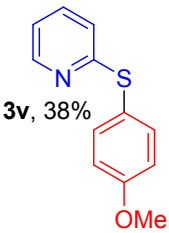
3s, 41%



3t, 12%

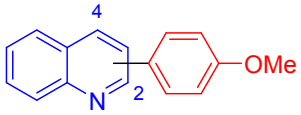


3u, 15%
2-aryl/4-aryl, 60:40

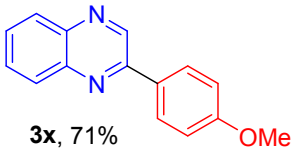


3v, 38%

obtained from pyridine-2-thiol



3w, 72%
2-aryl/4-aryl, 41:59



3x, 71%

Scheme 2. Evaluation of the reaction scope. All reactions were carried out on a scale of 7.5 mmol of **1a-g** and 0.5 mmol of **2a-r** in H_2O (1.5 mL). Isolated yields with ratio determined after column chromatography.

Among the aryldiazonium tetrafluoroborate salts tested for the direct arylation of the pyridine moiety, electron-donor (Scheme 2, **3l** and **3o**) and neutral-4-substituted aryldiazonium salts (Scheme 2, **3b** and **3c**) were more efficient than electron-acceptor-4-substituted groups (Scheme 2, **3d** and **3i**). However, the reaction with the aryldiazonium salt **2r**, which contains the π-donor group 4-$N(Me)_2$, provided the 2-arylated pyridine (**3r**) in only 14% yield, and the diazo-substituted product **6** in 13% yield.

In the work reported by Heinrich and co-workers (2016),[63] an aryldiazonium chloride salt containing the same 4-dimethylamino group was not successful in the radical arylation of 3-hydroxypyridine mediated by $TiCl_3$, which suggests incompatibility of this type of substrate with radical C–H arylation protocols.

Intriguingly, the aryldiazonium salts **2p** (R = 3-Ethyl) and **2q** (R = 2-Ethyl) also underwent substitution reactions by hydroxyl groups (from the solvent water) to give the phenols **4** and **5** in yields of 55% and 56%, respectively. The use of π-acceptor (NO_2) or donor (OMe) substituents at the 2 and 3 positions of the aryldiazonium ring decreased the yield of products compared with the same substituents at the 4-position of the diazonium salts. However, this effect was more pronounced for the methoxy donor substituent (Scheme 2, **3m** and **3n**) than for the nitro acceptor (Scheme 2, **3i**-**3k**). Furthermore, lower yields were observed when σ-acceptors (F and CF_3) groups were present at the 2 and 3- positions of the aryldiazonium rings (see Scheme 2, **3e** vs **3f** and **3g** vs **3h**).

Sakakura[64] reported that some diazonium salts such as 3-methoxybenzenediazonium (**2m**) and certain heteroarenediazonium tetrafluoroborates are known to decompose when dried, which may explain the observed low yield obtained

for biaryl **3m** (13%). Indeed, Heinrich and co-workers [63] also reported problems with the use of an aryldiazonium chloride containing the *meta*-methoxy group, which partially decomposed before the addition to the reaction mixture. In the case of compounds **3e**-**3h** bearing σ-acceptors (F and CF_3) groups, the difference in yields between the *ortho* and *meta* derivatives can be due to steric and/or electronic factors. However, we do not rule out the possibility that the yields of these and other reactions (such as Scheme 2, **3p**,**3q**) are correlated with the (photo)stability of the corresponding aryldiazonium salts. As well as the nature of the counter-ion, it is known that the substituent nature and position on the cation are of the greatest importance for the stability of the aryldiazonium salt.[65,66]

We also included additional *N*-heterocycles (Scheme 2) as scope with the 4-trifluoromethyl-pyridine (giving **3s** in 41% yield), 4-methoxy-pyridine (giving **3t** in 12% yield), 2-methoxipyridine (giving **3u** in 15% yield), pyridine-2-thiol (giving **3v** in 38% yield), quinoline (giving **3w** in 72% yield) and quinoxaline (giving **3x** in 71% yield). Overall, the substitued pyridines with electron-withdrawing and donating groups yielded produtcs from low to acceptable yields (12-41%). The pyridine-2-thiol yielded the product **3v** (38%) with the arylation in the thiol position and not in the aromatic ring. Both quinoline and quinoxaldine yielded arylated poducts in good yields (71-72%) demonstrating additional possibilities to apply this methodology.

Mechanistic Insights, and Counterpoints with Ru-photocatalyzed reactions

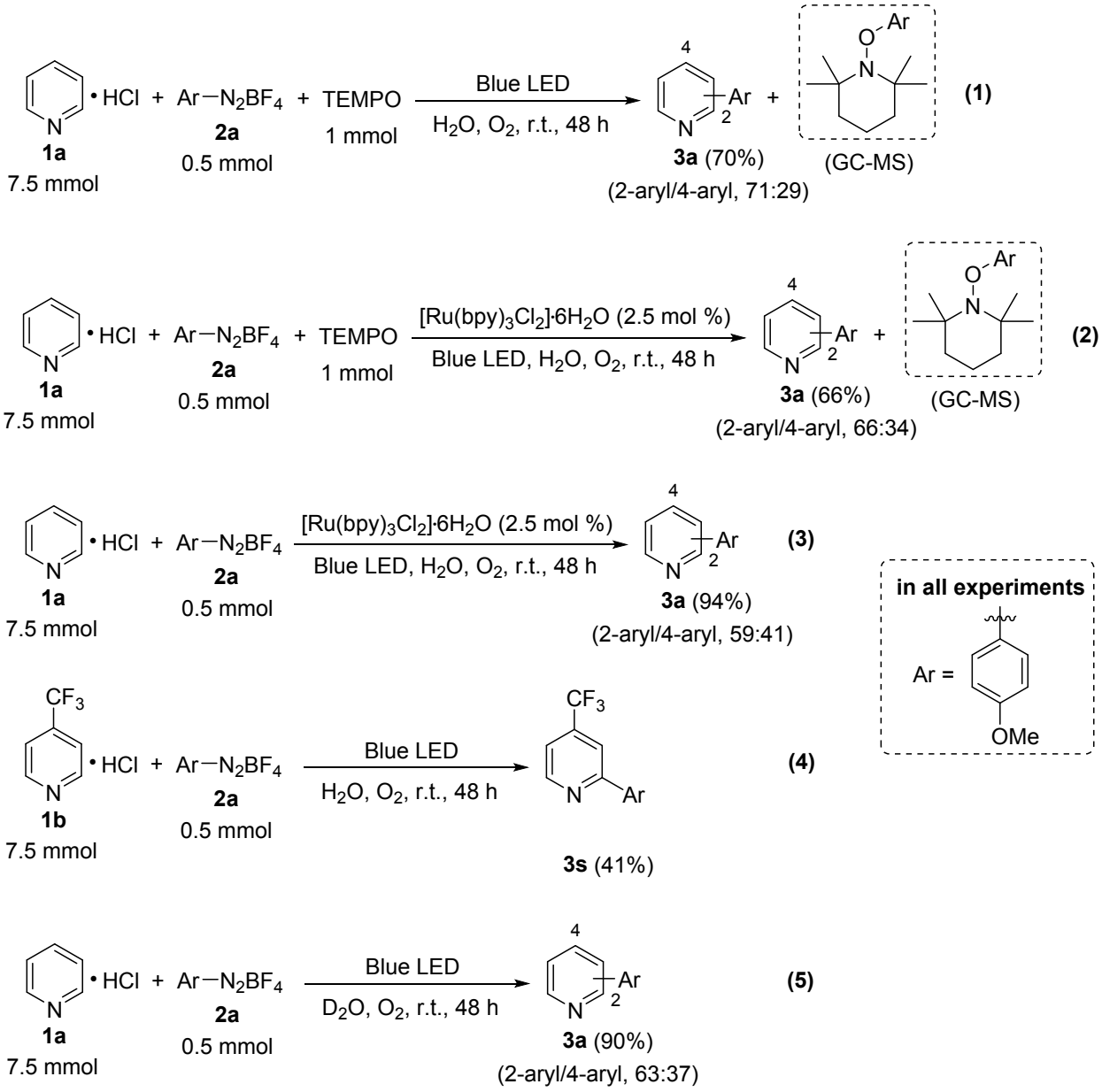
To gain some insights into the mechanism of this metal-free C–H photoarylation reaction, we conducted several control experiments with the substrates **1a** and **2a** and compared our results with the literature using Ru-photocatalysts (see Scheme 3). As

observed in our experiments performed in the dark (Table 1, entries 1 and 17) only traces of the 2-aryl-regioisomer **3a** were detected by GC-MS after 48 h, showing that the reaction is being promoted by blue LED visible-light. We also performed a reaction in the presence of 2 equiv. of the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and only partial inhibition of the reaction was observed (Scheme 3, Eq. 1). The aryl radical was trapped with TEMPO and was detected by GC-MS (see Figure S1, SI) and **3a** obtained in 70% yield (as against 96% yield, Table 1, entry 15, in the absence of TEMPO). This result suggests that the reaction involves radical intermediates, but complete radical trapping with full inhibition was not observed, probably due to the low solubility of TEMPO in water.

Subsequently, we tried to reproduce in our setup and optimized substrate proportions, the reaction between **1a** and **2a** reported by Xue and co-workers[41] using $Ru(bpy)_3Cl_2$ (2.5 mol%) in the presence of 2 equiv. of TEMPO. However, in our hands, the compound **3a** was obtained in 66% yield and only traces of the radical trapped with TEMPO was detected by CG-MS, against the 0% described by the before-mentioned authors (Scheme 3, Eq. 2 and Figure S2, SI). Furthermore, we tried to reproduce the same previous reaction without TEMPO (Scheme 3, Eq. 3) and obtained the compound **3a** in 94% yield. This result is statistically the same as compared to that reported in the mentioned literature (93%) by using the Ru-photocatalyst. However, this is also consistent with the yield obtained by us without photocatalyst (96%, Table 1, entry 15), showing that these photoarylation reactions work in 48 h (against the 60-80 h reported) independently of Ru-catalysts. It is important to highlight that the literature background reaction[41] use *p*-CF_3-pyridine (**1b**) with **2a** (Scheme 3, Eq. 4) mentions that only traces of the product **3s**

were formed. We obtained the product **3s** in 41% yield after 48 h, as opposed to the reported traces obtained by Xue and co-workers[41] after 60 h.

These results show an inconsistency between our data and the above-mentioned report, but these differences may be due to the different reagent proportions, as well as their use of 45W white fluorescent light bulbs against the 30W blue LEDs used in this study.



Scheme 3. Mechanistic investigations.

An additional control experiment was performed with deuterated water as solvent (Scheme 3, Eq. 5), obtaining **3a** in a comparable 90% yield and with no incorporation of deuterium, showing no hydrogen transfer.

In order to understand which intermediate is photoactive in this reaction (a photochemical intermediate such as a diazopyridinium salt or an EDA complex) we carried out several UV-Vis, ^{1}H and ^{1}H-^{15}N HMBC NMR studies. The literature indicates that the formation of colored charge-transfer (CT) complexes between the electron-poor aryldiazonium salts and aromatic hydrocarbons occurs spontaneously, presenting a progressive bathochromic (red) shift with the decrease of the ionization potential of these aromatic substrates.[67,68] We have successfully detected a new UV-Vis band by mixing **1a** and **2a** as demonstrated in Figure 2A, and confirmed a very close match between the new band (black line) and the blue LED emission (blue line) (Figure 2A).

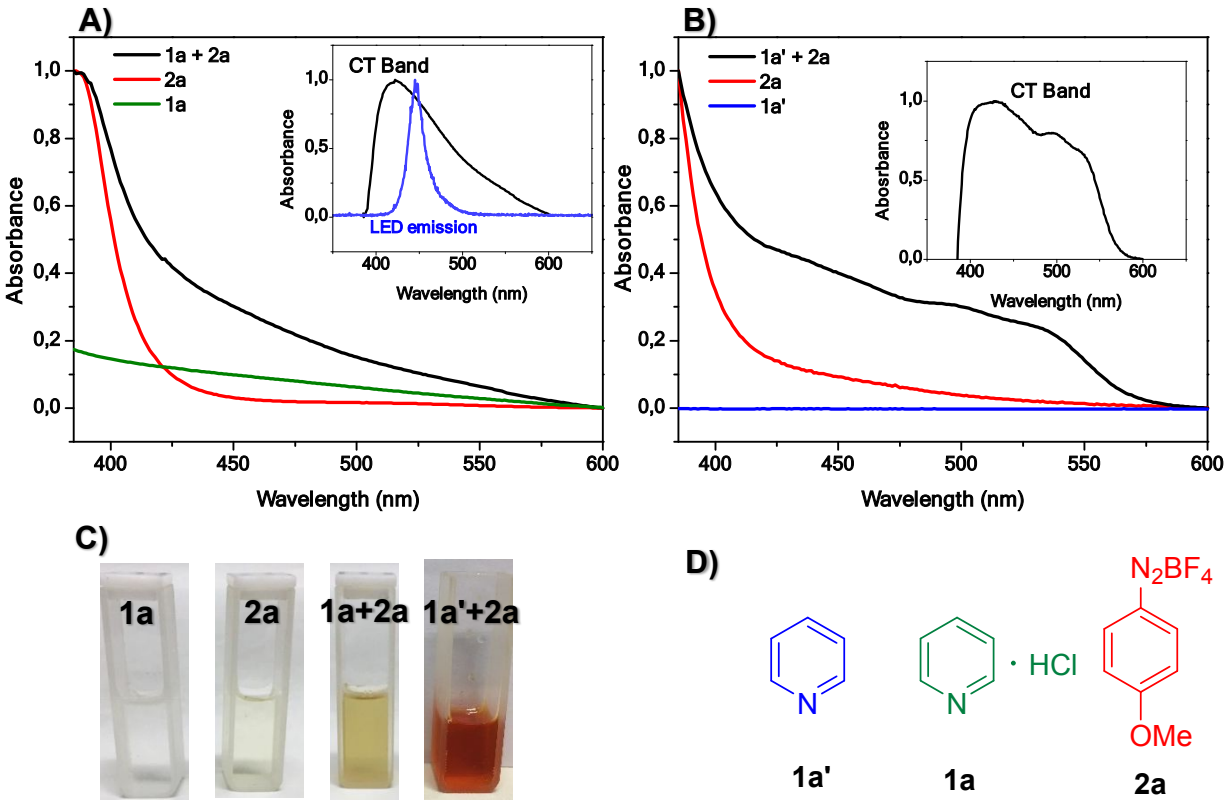


Figure 2. (A) UV-Vis absorption spectra of **1a** (3 mmol), **2a** (0.2 mmol), and the mixture of **1a** and **2a** at 2 and 0.13 mM in H_2O, respectively. Inset: charge transfer band (CT) of

(**1a** + **2a**) EDA complex. (B) UV-Vis absorption spectra in NaCl solution (1M) for **1a'**, **2a** and their mixture of **1a'** and **2a** at 2 and 0.13 mM. Inset: the charge transfer band (CT) of (**1a'** + **2a**) EDA complex. (C) Images of the solutions **1a**, **2a**, **1a** + **2a** and **1a'** +**2a**. D) molecular structure of the species.

These first studies by UV-Vis (Figure 2A) are consistent with the occurrence of an EDA complex. However, it is well-known in the literature that EDA complexes are supramolecular structures.[69] In the case of mixtures of diazonium salts and pyridines the literature describes the occurrence of diazopyridinium salts at low temperatures,[70] which are discrete structures and could not be considered as EDA complexes. In order to find more data to confirm the real photochemical intermediate of this study, we performed one experiment with the diazonium salt **2a** in the presence of NaCl instead of pyridinium chloride, obtaining exactly the same UV-Vis band of the diazonium salt **2a** and showing that the chloride ion is not able to form an EDA with **2a**. In addition, an UV-Vis experiment with the diazonium salt **2a** and free pyridine (**1a'**) was carried out showing a very similar new UV-Vis band with an evident more colored solution (Figure 2B and 2C). We were able to conclude that there is an evident interaction between pyridine and the diazonium salt moieties, which is present when mixing pyridine.HCl (**1a**) and the diazonium salt **2a**. Due to the acid-base equilibrium the concentration of free pyridine is low and the EDA formed is more discrete (low concentration). However, in the presence of high concentrations of free pyridine **1a'** the occurrence of the EDA complex is more evident (Figure 2B). It is important to highlight that our methodology deals with the formation of

an EDA, but also with a relative concentration of protonated pyridine or heterocycle in order to have the radical acceptor activated.

We also performed ^{1}H NMR experiments in D_2O analysing **1a** and **2a** individually and mixtures of both in diferent proportions. First, aggregation studies at high concentrations (from 35-280 mM) of **1a** and **2a** were carried out by ^{1}H NMR (Figure S3 – Supporting Information), and no aggregation in solution was detected even at high concentrations (280 mM); it is well-known that aggregation on aromatic compounds in solutions can dramatically change the chemical shifts.[71]

In the ^{1}H NMR analysis of the mixture of both **1a** and **2a** (1:1 equiv.) in D_2O we observed a slight protection of the ^{1}H signals of the diazonium salt **2a** and a slight deprotection of the ^{1}H signals in **1a** (Figure 3). Similarly, the mixture of the diazonium salt **2a** and free pyridine (**1a'**) yielded ^{1}H NMR analyses with protected signals for the diazonium salt **2a** and deprotected signals for the free pyridine (**1a'**) in both 1:1 and 1:5 molar proportions (Figure 4). This indicates an electron-donor effect by the pyridine nucleus and an electron-acceptor effect by the diazonium salt moiety. It is important to highlight that the protection/deprotection effects are more relevant in the 1:5 molar ratio experiment, which is in aggrement with the supramolecular properties of the EDA complexes. Additional experiments of ^{1}H-^{15}N HMBC were performed (Figure S7 - Supporting Information) and from the results only ^{1}H-^{15}N correlations of individual **1a'** and **2a** were found by mixing these starting materials in D_2O with no photochemically active intermediate such as a diazopyridinium salt detected in these reaction conditions.

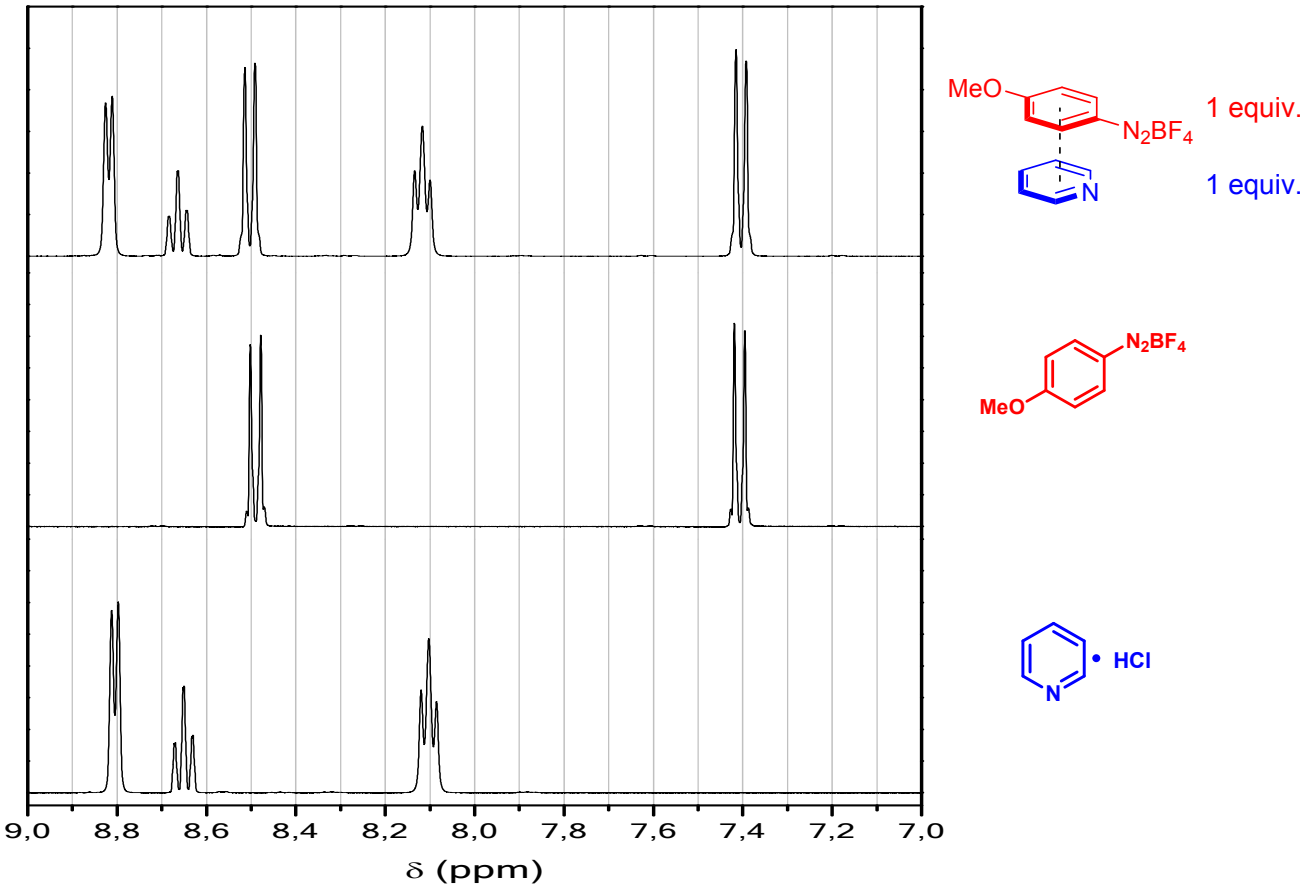


Figure 3: ^{1}H NMR spectrum for **1a** (at 35 mM), **2a** (at 35 mM) and their mixture 35 mM (1:1 equiv.) in D_2O.

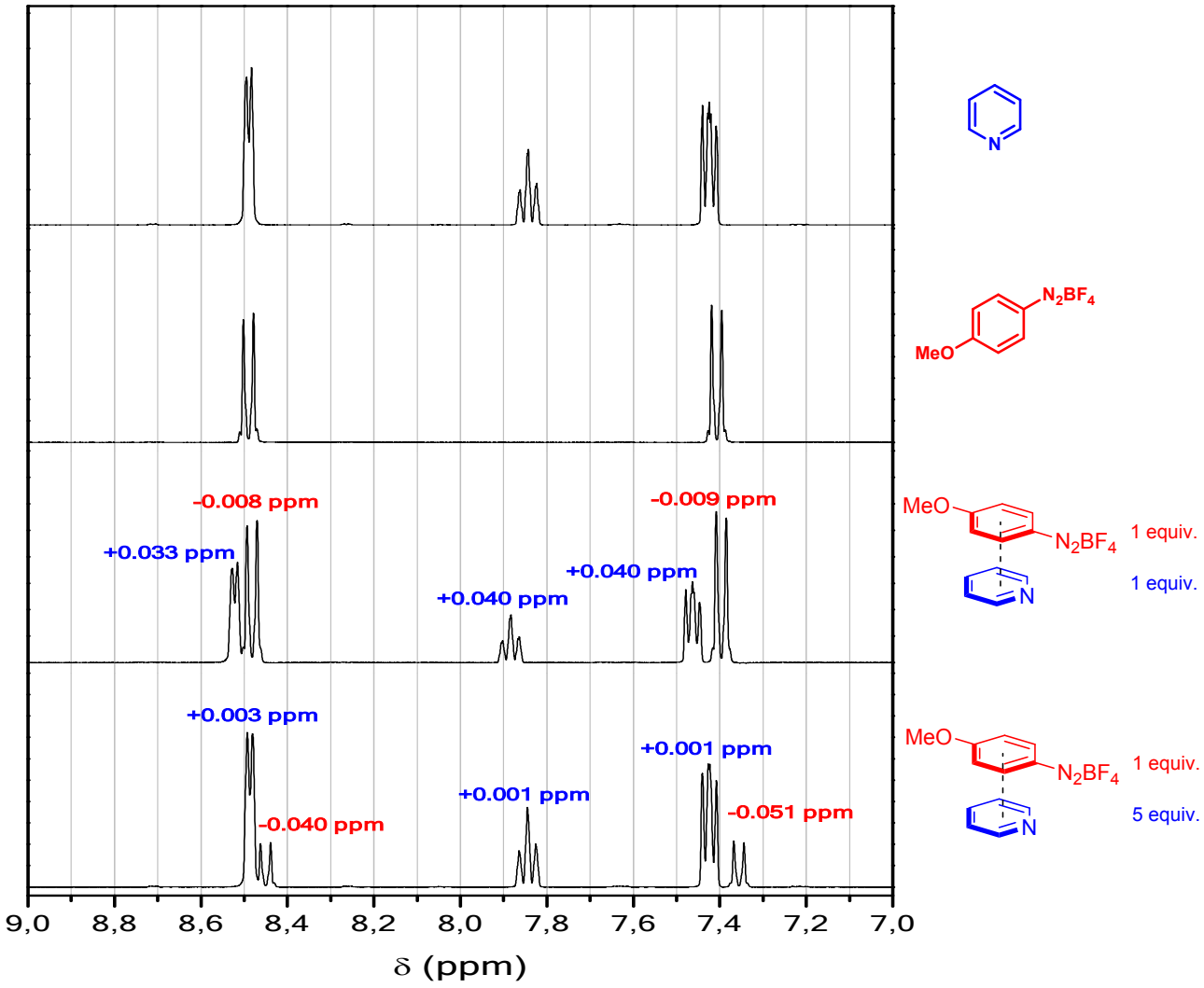
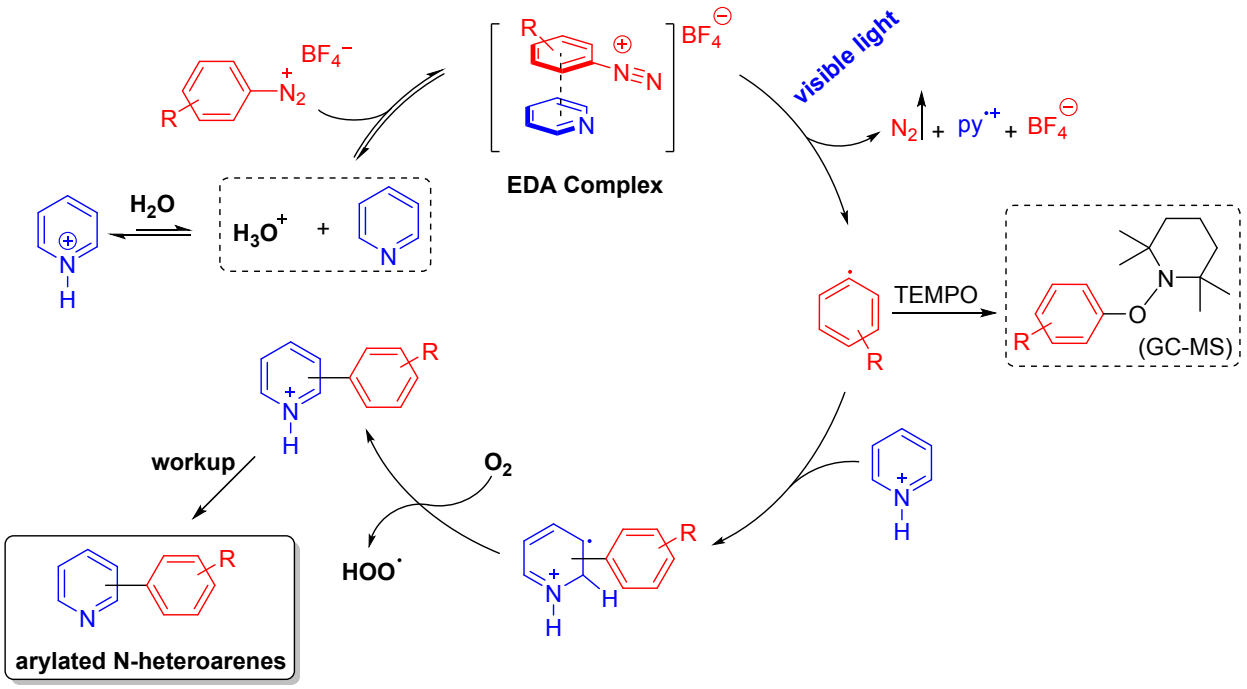


Figure 4: ^{1}H NMR spectrum for **1a'** (at 35 mM), **2a** (at 0.18 mM) and their mixture (1:1equiv. at 35 mM and 1:5 equiv, 35: 175 mM) in D_2O.

Based on these results we propose a plausible mechanism for the visible-light-induced direct C–H arylation of pyridines (Scheme 4). Initially, the aryldiazonium salt reversibly combines with free pyridine/heterocycle generating the EDA complex which absorbs blue light, and then the rupture in the excited state yields the aryl radical.[72,73] Then, the aryl radical reacts with the pyridinium salt to form a new radical intermediate. The latter is subsequently re-aromatized by reaction with oxygen gas. It is relevant to

highlight that we have confirmed that the oxygen atmosphere has an important role in improving the yields.[45] Finally, aqueous work-up liberates the desired arylated heterocycles.



Scheme 4. Proposed mechanism for the visible-light induced direct C–H arylation of pyridines.

Conclusion

We have developed a metal-free methodology for the photoarylation of pyridines and other heterocycles in water, using a very simple photoreactor setup. The scope of the diazonium salt is presented showing the relative strength of this methodology when both electron-withdrawing and donating groups are attached to the diazonium salts (*ortho*, *meta* and *para* positions). Mechanistic investigations were carried out giving support for the proposed mechanism and the occurence of an EDA complex.

EXPERIMENTAL SECTION

General Information

All commercial reagents were used without further purification. Aryldiazonium salts were prepared according to the literature procedure.[74] All the reactions were carried out under an oxygen atmosphere. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm silica plates, using short-wave UV light (254 nm or 365 nm) for visualization. Flash column chromatography was performed on silica gel (70 – 230 mesh). NMR spectra were recorded on a Bruker Avance 400 MHz instrument, and chemical shifts for ^{1}H and $^{13}C\{^{1}H\}$ NMR are reported in ppm relative to TMS as internal reference. All coupling constants (*J* values) are reported in Hertz (Hz). The following abbreviations were used to describe NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. High-resolution mass spectra (HRMS) were performed on Agilent LC-6545, Q-TOF MS with Jet Stream ESI ionization. UV-Vis absorption spectra were recorded on a Perkin Elmer Lambda 25 UV-visible absorption spectrophotometer.

General Procedures

Aryldiazonium salt preparation:

To a solution of aniline (10 mmol) in distilled H_2O (4 mL), aq. HBF_4 50 wt. % was added (3.4 mL) and the mixture was stirred while cooled to 0^{o}C. Subsequently, a solution of $NaNO_2$ (10 mmol, 690 mg) in H_2O (2 mL) was added dropwise. After addition, the reaction mixture was stirred for 45 min and then the solid filtered off under vacuum. The precipitate was re-dissolved in a minimum amount of acetone (ca 5-8 mL). Diethyl ether was added until precipitation of the diazonium tetrafluoroborate. The solid was filtered off and washed

with diethyl ether and dried under vacuum. The NMR data were consistent with those previously reported.[75]

Synthetic methodology:

To a test tube (borosilicate, 10 mm internal diameter and 1 mm thick walls) *N*-heterocycle hydrochloride salt (**1a-g**) (7.5 mmol, 15 equiv.) was added to 1.5 mL of H_2O. The test tube was then sonicated to remove the solubilized air and after saturated with pure O_2 by bubbling this gas for 10 min. The aryldiazonium salt (**2a**-**r**) (0.5 mmol, 1 equiv.) was quickly added, the tube was closed and sealed with Teflon tape. The reaction mixture was stirred and irradiated using a homemade batch photoreactor (30W blue LEDs) under an oxygen atmosphere (balloon) at r.t. for 48h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 20 mL). The organic extracts were washed with brine (1 × 10 mL), dried over $MgSO_4$, filtered, and the solution concentrated under vacuum. The crude reaction product was chromatographed on silica gel (70–230 mesh) using EtOAc/hexane mixtures of increasing polarity to afford 2-aryl/4-aryl substituted pyridines (**3a**-**v**), 2-aryl/4-arylquinoline (**3w**) and 2-aryl-quinoxaline (**3x**) in yields ranging from 12 to 96%.

Experimental Data

*2-(4-methoxyphenyl)pyridine – 2-aryl (**3a**):* The compound 2-aryl (**3a**) (known compound)[76] was obtained following the general procedure. It was obtained in 68% yield (0.341 mmol, 63.2 mg) as a yellow solid after purification on silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 51–53 °C (lit.[23] mp 53–55 °C).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (m, 1 H), 7.95 (d, *J* = 9.0 Hz, 2 H), 7.74−7.64

(m, 2 H), 7.17 (ddd, *J* = 7.1 ,4.9 ,1.4 Hz, 1 H), 7.00 (d, *J* = Hz, 9.0 Hz, 2 H), 3.86 (s, 3 H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 160.5, 157.1, 149.5, 136.7, 132.0, 128.2, 121.4, 119.8, 114.1, 55.4.

*4-(4-methoxyphenyl)pyridine – 4-aryl (**3a**):* The compound 4-aryl (**3a**) (known compound)[76] was obtained following the general procedure. It was obtained in 28% yield (0.138 mmol, 25.5 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 91–94 °C (lit.[77] mp 94–96 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 6.2 Hz, 2 H), 7.60 (*d*, *J* = 9.0 Hz, 2 H), 7.47 (d, *J* = 6.2 Hz, 2 H), 7.01 (d, *J* = 9.0 Hz, 2 H), 3.87 (s, 3 H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 160.5, 150.2, 147.8, 130.4, 128.2, 121.1, 114.6, 55.4.

*2-phenylpyridine – 2-aryl (**3b**):* The compound 2-aryl (**3b**) (known compound)[78] was obtained following the general procedure. It was obtained in 44% yield (0.219 mmol, 34.0 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 8/2 (v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71-8.68 (m, 1H), 7.99 (d, *J* = 7.0 Hz, 2H), 7.78-7.71 (m, 2H), 7.50-7.45 (m, 2H), 7.44-7.39 (m, 1H), 7.23 (ddd, *J* = 6.8, 4.8, 2.0, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 157.5, 149.7, 139.4, 136.8, 129.0, 128.8, 126.9, 122.1, 120.6.

*4-phenylpyridine – 4-aryl (**3b**):* The compound 4-aryl (**3b**) (known compound)[79,80] was obtained following the general procedure. It was obtained in 18% yield (0.090 mmol, 13.9 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 8/2 (v/v)). Mp: 62–64 °C (lit.[80] mp 67–68 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 5.6, Hz, 2H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.46-7.34

(m, 5H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 150.3, 148.4, 138.2, 129.1, 129.0, 127.0, 121.7.

*2-(4-chlorophenyl)pyridine – 2-aryl (**3c**):* The compound 2-aryl (**3c**) (known compound)[80] was obtained following the general procedure. It was obtained in 54% yield (0.272 mmol, 51.6 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)).)). Mp: 46 – 48 °C (lit.[80] mp 44 – 45 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (ddd, *J* = 4.8, 1.8, 1.1 Hz, 1H), 7.94 (d , *J* = 9.0 Hz, 2H), 7.76 (ddd, *J* = 8.0, 7.4, 1.8 Hz, 1H), 7.72-7.68 (m, 1H), 7.45 (d, *J* = 9.0 Hz, 2H), 7.25 (ddd, *J* = 7.4, 4.8, 1.3 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 156.2, 149.8, 137.8, 136.9, 135.1, 129.0, 128.1, 122.4, 120.4.

*4-(4-chlorophenyl)pyridine – 4-aryl (**3c**):* The compound 4-aryl (**3c**) (known compound)[80] was obtained following the general procedure. It was obtained in 26% yield yield (0.128 mmol, 24.3 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 70 – 71 °C (lit.[80] mp 70 – 71 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (s, 2H), 7.58 (d, *J* = 8.9 Hz, 2H), 7.50-7.45 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 150.4, 147.1, 136.6, 135.4 129.4, 128.3, 121.5.

*2-(4-fluorophenyl)pyridine – 2-aryl (**3d**):* The compound 2-aryl (**3d**) (known compound)[23,81] was obtained following the general procedure. It was obtained in 31% yield (0.156 mmol, 27.1 mg) as a white solid after purification over silica gel column chromatography (Dichloromethane/EtOAc = 9.5/0.5 (v/v)). Mp: 35–37 °C (lit.[23] mp 39–41 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.00-7.95 (m, 2H), 7.75 (ddd, *J* = 8.0, 7.4, 1.8 Hz, 1H), 7.70-7.66 (m, 1H), 7.22 (ddd, *J* = 7.4, 4.8, 1.2 Hz,

1H). 7.19-7.12 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 163.5 (d, J_{CF} = 248 Hz), 156.5, 149.7, 136.8, 135.5, 128.7, 122.1, 120.2, 115.8, 115.6.

*4-(4-fluorophenyl)pyridine – 4-aryl (**3d**):* The compound 4-aryl (**3d**) (known compound)[82,83] was obtained following the general procedure. It was obtained in 22% yield (0.109 mmol, 19.0 mg) as a white solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). 112–114 °C (lit.[82] mp 116–118 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 4.6 Hz, 2 H), 7.66 - 7.58 (m, 2 H), 7.50-7.44 (m, 2 H), 7.22-7.14 (m, 2 H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 163.5 (d, $J_{C\text{-}F}$ = 248 Hz), 150.2, 147.4, 134.2, 134.1, 128.8, 128.7, 121.5, 116.3, 116.1.

*2-(3-fluorophenyl)pyridine – 2-aryl (**3e**):* The compound 2-aryl (**3e**) (known compound)[84] was obtained following the general procedure. It was obtained in 36% yield (0.178 mmol, 30.8 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). ^{1}H NMR (400 MHz, acetone-d6): δ 8.70 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.94-7.88 (m, 2H), 7.57-7.51 (m, 1H), 7.38 (ddd, *J* = 7.4, 4.8, 1.1 Hz, 1H), 7.21 (dddd, *J* = 8.6, 8.2, 2.6, 0.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, acetone-d6): δ 164.2 (d, J_{CF} = 242 Hz), 156.1, 150.6, 142.7 (d, J_{CF} = 7 Hz), 138.0, 131.4 (d, J_{CF} = 8 Hz), 123.9, 123.3, 121.2, 116.4 (d, J_{CF} = 21 Hz), 114.0 (d, J_{CF} = 23 Hz).

*4-(3-fluorophenyl)pyridine – 4-aryl (**3e**):* The compound 4-aryl (**3e**) (known compound)[85] was obtained following the general procedure. It was obtained in 22% yield (0.109 mmol, 18.9 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, *J* = 6.0 Hz, 2H), 7.51 – 7.41 (m, 4H), 7.36 – 7.32 (m, 1H), 7.18 – 7.12 (m, 1H). $^{13}C\{^{1}H\}$ NMR

(100 MHz, $CDCl_3$): δ 164.4,162.0, 150.4, 147.1, 140.3 (d, J_{CF} = 8.0 Hz), 130.7 (d, J_{CF} = 8 Hz), 122.7, 121.6, 115.9 (d, J_{CF} = 21 Hz), 114.0 (d, J_{CF} = 22 Hz).

*2-(2-fluorophenyl)pyridine – 2-aryl (**3f**):* The compound 2-aryl (**3f**) (known compound)[86] was obtained following the general procedure. It was obtained in 20% yield (0.098 mmol, 16.9 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 7.92 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.78-7.68 (m, 2H), 7.34 (dddd, *J* = 8.3, 7.3, 5.0, 1.9, 1H), 7.24 (ddd, *J* = 7.3, 4.8, 1.4 Hz, 1H), 7.20 (ddd, *J* = 7.8, 7.3, 1.2 Hz, 1H), 7.12 (dddd, *J* = 11.7, 8.2, 1.2, 0.3 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, acetone-d6): δ 161.4 (d, J_{CF} = 251 Hz), 153.9, 150.7, 137.4, 132.0, 131.5 (d, J_{CF} = 8 Hz), 128.3 (d, J_{CF} = 11 Hz), 125.4, 125.1 (d, J_{CF} = 9 Hz), 123.6, 116.9 (d, J_{CF} = 23 Hz).

*4-(2-fluorophenyl)pyridine – 4-aryl (**3f**):* The compound 4-aryl (**3f**) (new compound) was obtained following the general procedure. It was obtained in 11% yield (0.054 mmol, 9.4 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 62–64 °C. ^{1}H NMR (400 MHz, acotone-d6): δ 8.55 (d, *J* = 5.9 Hz, 2H), 7.50 (dt, *J* = 7.8, 0.3 Hz, 1H), 7.46-7.42 (m, 2H), 7.39 (dddd, *J* = 8.2, 7.3, 5.1, 1.8, 1H), 7.23 (dt, *J* = 7.3, 1.2 Hz, 1H), 7.17 (dddd, *J* = 11.2, 8.3, 1.2, 0.3 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, acetone-d6): δ 160.6 (d, J_{CF} = 248 Hz), 150.9, 143.9, 131.8 (d, J_{CF} = 9 Hz), 131.5, 127.0 (d, J_{CF} = 13 Hz), 126.0 (d, J_{CF} = 4 Hz), 124.4, 117.1 (d, J_{CF} = 21 Hz). HRMS-ESI-TOF: *m/z* calcd for $C_{11}H_8FN$ $[M+H]^+$ 174.0714, found 174.0712.

*2-(3-(trifluoromethyl)phenyl)pyridine – 2-aryl (**3g**):* The compound 2-aryl (**3g**) (known compound)[87] was obtained following the general procedure. It was obtained in 31% yield

(0.154 mmol, 34.5 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 8.30-8.26 (m, 1H), 8.21-8.15 (m, 1H), 7.84-7.75 (m, 2H), 7.70-7.65 (m, 1H), 7.60 (tt, *J* = 7.8, 0.7 Hz, 1H), 7.30 (ddd, J = 6.9, 4.8, 1.6 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.9, 149.9, 140.1, 137.0, 131.2 (q, J_{CF} = 32.2 Hz), 130.0, 129.2, 128.2, 125.5 (q, J_{CF} = 4 Hz), 123.8 (q, J_{CF} = 4 Hz), 122.8, 120.6.

*4-(3-(trifluoromethyl)phenyl)pyridine – 4-aryl (**3g**):* The compound 4-aryl (**3g**) (known compound)[88] was obtained following the general procedure. It was obtained in 18% yield (0.093 mmol, 20.7 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, *J* = 5.3 Hz, 2 H), 7.91-7.85 (m 1H), 7.85-7.89 (m, 1H), 7.71-7.69 (m, 1H), 7.67-7.59 (m 1H), 7.53 (d, *J* = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.4, 147.0, 139.0, 130.3, 131.6 (d, J_{CF} = 33 Hz), 129.7, 125.7 (d, J_{CF} = 5 Hz), 123.9 (d, J_{CF} = 5 Hz), 121.7.

*2-(2-(trifluoromethyl)phenyl)pyridine – 2-aryl (**3h**):* The compound 2-aryl (**3h**) (known compound)[81] was obtained following the general procedure. It was obtained in 23% yield (0.113 mmol, 25.4 mg) as a yellow oil after purification over silica gel column chromatography (Toluene/EtOAc = from 9.5/0.5 (v/v) to 9/1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 7.80–7.72 (m, 2H), 7.66-7.59 (m, 1H), 7.57-7.49 (m, 2H), 7.46–7.41 (m, 1H), 7.32, (ddd, *J* = 7.5, 4.8 , 1.0, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.8, 149.2, 140.0, 136.0, 131.6, 131.5, 128.3, 126.3 (q, J_{CF} = 5 Hz), 125.4, 124.0, 122.7, 122.5.

*2-(4-nitrophenyl)pyridine – 2-aryl (**3i**):* The compound 2-aryl (**3i**) (known compound)[89] was obtained following the general procedure. It was obtained in 42% yield (0.210 mmol, 42.0 mg) as a white solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 132–133 °C (lit.[90] mp 130–131 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 8.34 (d, *J* = 9.0 Hz, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 7.87-7.80 (m, 2H), 7.31 (ddd, *J* = 6.5, 4.8, 2.1, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.9, 150.1, 148.2, 145.3, 137.2, 127.7, 124.0, 123.6, 121.2.

*4-(4-nitrophenyl)pyridine – 4-aryl (**3i**):* The compound 4-aryl (**3i**) (known compound)[91] was obtained following the general procedure. It was obtained in 24% yield (0.120 mmol, 24.0 mg) as a white solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 120 – 123 °C (lit.[90] mp 122 – 124 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, *J* = 3.8 Hz, 2H), 8.36 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.9 Hz, 2H), 7.56-7.52 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.7, 148.2, 146.0, 144.5, 128.0, 124.4, 121.8.

*2-(3-nitrophenyl)pyridine – 2-aryl (**3j**):* The compound 2-aryl (**3j**) (known compound)[92] was obtained following the general procedure. It was obtained in 30% yield (0.15 mmol, 29.9 mg) as an yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 72–73 °C (lit.[92] mp 70–72 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.87 (t, *J* = 1.9 Hz, 1H), 8.77-8.71 (m, 1H), 8.37 (ddd, *J* = 7.7, 1.6, 1.0 Hz, 1H), 8.27 (ddd, J = 8.2, 2.2, 1.0 Hz, 1H), 7.87-7.80 (m, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.33 (ddd, *J* = 7.2, 4.8, 2.2, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.8, 150.0, 148.8, 141.0, 137.2, 132.7, 129.7, 123.6, 123.3, 121.8, 120.6.

*4-(3-nitrophenyl)pyridine – 4-aryl (**3j**):* The compound 4-aryl (**3j**) (known compound)[92] was obtained following the general procedure. It was obtained in 19% yield (0.096 mmol, 19.2 mg) as a orange solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 103–105 °C (lit.[92] mp 109–110 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81−8.70 (m, 2H), 8.51 (t, *J* = 1.8 Hz, 1H), 8.32 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 7.98 (ddd, *J* = 7.7, 1.8, 1.0 Hz, 1H), 7.70 (t, *J* = 7.9 Hz, 1H), 7.60−7.54 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.6, 148.9, 145.9, 139.9, 132.9, 130.3, 124.3, 123.8, 122.0, 121.6.

*2-(2-nitrophenyl)pyridine – 2-aryl (**3k**):* The compound 2-aryl (**3k**) (known compound)[93] was obtained following the general procedure. It was obtained in 31% yield (0.153 mmol, 30.6 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 71 – 72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.88-8.85 (m, 1H), 8.76-8.73 (m, 1H), 8.38 (ddd, *J* = 7.8, 1.7, 1.0 Hz, 1H), 8.27 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 7.87-7.80 (m, 2H), 7.69−7.63 (m, 1H), 7.34 (ddd, *J* = 6.4, 4.8, 2.3 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.8, 150.0, 148.8, 141.0, 137.2, 132.7, 129.7, 123.6, 123.3, 121.8, 120.6.

*4-(2-nitrophenyl)pyridine – 4-aryl (**3k**):* The compound 4-aryl (**3k**) (known compound)[94] was obtained following the general procedure. It was obtained in 21% yield (0.103 mmol, 20.7 mg) as a yellon solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 51–52 °C (lit.[94] mp 49–50 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, *J* = 5.8 Hz, 2H), 8.53-8.50 (m, 1H), 8.32 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 7.97 (ddd, *J* = 7.7, 1.8, 1.0 Hz, 1H), 7.73−7.68 (m, 1H), 7.59-7.55 (m,

2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.6, 148.9, 146.0, 139.9, 132.9, 130.3, 123.8, 122.0, 121.6.

*2-(p-tolyl)pyridine– 2-aryl (**3l**):* The compound 2-aryl (**3l**) (known compound)[80] was obtained following the general procedure. It was obtained in 54% yield (0.270 mmol, 45.8 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 8/2 (v/v)). ^1H NMR (400 MHz, $CDCl_3$): δ 8.70-8.64 (m, 1H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.76-7.67 (m, 2H), 7.30-7.26 (m, 2H), 7.20 (ddd, *J* = 6.8, 4.8, 1.9 Hz, 1H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 157.5, 149.6, 139.0, 136.7, 136.6, 129.5, 126.8, 121.8, 120.3, 21.3.

*4-(p-tolyl)pyridine – 4-aryl (**3l**):* The compound 4-aryl (**3l**) (known compound)[80] was obtained following the general procedure. It was obtained in 26% yield (0.130 mmol, 22.0 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 8/2 (v/v)). Mp: 86–88 °C (lit.[80] mp 89–90 °C). ^1H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.7 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.52-7.47 (m, 2H), 7.32-7.28 (m, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.2, 148.2, 139.2, 135.2, 129.9, 126.8, 121.4, 21.2.

*2-(3-methoxyphenyl)pyridine – 2-aryl (**3m**):* The compound 2-aryl (**3m**) (known compound)[77] was obtained following the general procedure. It was obtained in 9% yield (0.043 mmol, 8.00 mg) as an oil after purification over silica gel column chromatography (Hexane/2-propanol = from 9.5/0.5 (v/v)). ^1H NMR (400 MHz, $CDCl_3$): δ 8.68 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 7.80–7.70 (m, 2H), 7.59 (dd, *J* = 2.5, 1.7 Hz, 1H), 7.54 (ddd, *J* = 7.7, 1.6, 1.0, Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.24 (ddd, *J* = 6.7, 4.8, 1.7 Hz 1H), 6.98 (ddd,

J = 8.2, 2.5, 1.0 Hz, 1H), 3.90 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 160.0, 157.2, 149.6, 140.8, 136.8, 129.8, 122.3, 120.8, 119.3, 115.2, 112.0, 55.4.

*4-(3-methoxyphenyl)pyridine – 4-aryl (**3m**):* The compound 4-aryl (**3m**) (known compound)[95] was obtained following the general procedure. It was obtained in 4% yield (0.022 mmol, 4.00 mg) as an oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). ^1H NMR (400 MHz, $CDCl_3$): δ 8.71-8.47 (m, 2H), 7.47-7.40 (m, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.16 (ddd, *J* = 7.6, 1.7, 0.9 Hz, 1H), 7.09 (dd, *J* = 2.4, 1.7 Hz, 1H), 6.92 (ddd, *J* = 6.9, 2.4, 0.9 Hz, 1H), 3.81 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 160.2, 150.1, 148.4, 139.6, 130.2 121.8, 119.4, 114.4, 112.8, 55.4.

*2-(2-methoxyphenyl)pyridine – 2-aryl (**3n**):* The compound 2-aryl (**3n**) (known compound)[84] was obtained following the general procedure. It was obtained in 38% yield (0.192 mmol, 35.5 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). ^1H NMR (400 MHz, $CDCl_3$): δ 8.63 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.73 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.68 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.62(ddd, *J* = 8.0, 7.6, 1.8 Hz, 1H), 7.30 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 1H), 7.13 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.00 (dt, *J* = 7.5, 1.1 Hz, 1H), 6.93 (dd, *J* = 8.3, 1.0 Hz, 1H), 3.78 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 156.9, 156.1, 149.4, 135.6, 131.2, 129.9, 129.2, 125.1, 121.7, 121.0, 111.4, 55.6.

*4-(2-methoxyphenyl)pyridine – 4-aryl (**3n**):* The compound 4-aryl (**3n**) (known compound)[77,95] was obtained following the general procedure. It was obtained in 19% yield (0.098 mmol, 18.1 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 56–59 °C (lit.[77] mp 63–65 °C). ^1H NMR (400 MHz, $CDCl_3$): δ 8.63 (d, *J* = 6.0 Hz, 2H), 7.53-7.49 (m, 2H), 7.40

(ddd, *J* = 8.3, 7.4, 1.7 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.07 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.03-7.00 (m, 1H), 3.85 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 156.5, 149.1, 146.4, 130.4, 130.2, 127.7, 121.1, 111.4, 55.6.

*2-(4-ethylphenyl)pyridine – 2-aryl (**3o**):* The compound 2-aryl (**3o**) (known compound)[96] was obtained following the general procedure. It was obtained in 51% yield (0.253 mmol, 46.4 mg) as a yellow oil after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 8/2 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.76-7.68 (m, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.20 (ddd, *J* = 6.5, 4.8, 2.0 Hz, 1H), 2.71 (q, *J* = 7.7 Hz, 2H), 1.27 (t, *J* = 7.7 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 157.5, 149.6, 145.3, 136.9, 136.7, 128.3, 126.9, 121.8, 120.3, 28.7, 15.5.

*4-(4-ethylphenyl)pyridine – 4-aryl (**3o**):* The compound 4-aryl (**3o**) (new compound) was obtained following the general procedure. It was obtained in 24% yield yield (0.120 mmol, 22.0 mg) as a white solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 8/2 (v/v)). Mp: 49–50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 6.0 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 6.0 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.6 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 150.1, 148.3, 145.6, 135.4, 128.7, 126.9, 121.5, 28.6, 15.5. HRMS-ESI-TOF: *m/z* calcd for $C_{13}H_{13}N$ $[M+H]^+$ 184.1121, found 184.1119.

*N,N-dimethyl-4-(pyridin-2-yl)aniline – 2-aryl (**3r**):* The compound 2-aryl (**3r**) (known compound)[81,97] was obtained following the general procedure. It was obtained in 14% yield (0.068 mmol, 13.6 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 90–91 °C (lit.[97] mp 91–

92 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65-8.58 (m, 1H), 7.92 (d, *J* = 9.0 Hz, 2H), 7.71-7.62 (m, 2H), 7.10 (ddd, *J* = 6.7, 4.9, 1.7 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 2H), 3.02 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.5, 151.1, 149.2, 136.7, 127.8, 127.0, 120.6, 119.2, 112.2, 40.4.

*2-(4-methoxyphenyl)-4-(trifluoromethyl)pyridine – 2-aryl (**3s**):* The compound 2-aryl (**3s**) (known compound)[41] was obtained following the general procedure. It was obtained in 41% yield (0.204 mmol, 51.6 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = 9/1 (v/v)). Mp: 45–46 °C (lit.[41] mp 43–44 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.81 (d, *J* = 5.1 Hz, 1H), 7.99 (d, *J* = 9.0 Hz, 2H), 7.86 (quint, 0.7 H), 7.38 (ddd, *J* = 5.1, 1.6, 0.7 Hz, 1H), 7.02 (d, *J* = 9.0 Hz, 2H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 161.1, 158.4, 150.5, 139.0 (q, $J_{C\text{-}F}$ = 33.5 Hz), 130.6, 128.4, 123.0, (q, $J_{C\text{-}F}$ = 274.1 Hz), 116.7 (q, $J_{C\text{-}F}$ = 3.0 Hz), 115.2 (q, $J_{C\text{-}F}$ = 3.5 Hz), 114.3, 55.4.

*4-methoxy-2-(4-methoxyphenyl)pyridine – 2-aryl (**3t**):* The compound 2-aryl (**3t**) (known compound)[98] was obtained following the general procedure. It was obtained in 12% yield (0.061 mmol, 13.2 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = 7/3 (v/v)). Mp: 62 – 64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.48 (d, *J* = 5.7 Hz, 1H), 7.92 (d, *J* = 9.0 Hz, 2H), 7.17 (d, *J* = 2.3 Hz, 1H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.72 (dd, *J* = 5.7, 2.3 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 166.4, 160.5, 158.9, 150.8, 132.0, 128.2, 114.0, 107.6, 106.0, 55.4, 55.1.

*2-methoxy-6-(4-methoxyphenyl)pyridine – 2-aryl (**3u**):* The compound 2-aryl (**3u**) (known compound)[99] was obtained following the general procedure. It was obtained in 9% yield (0.047 mmol, 10.2 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 8/2 (v/v) to 6/4 (v/v)). Mp: 122–124 °C (lit.[99] mp

120–121 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.00 (d, *J* = 9.0 Hz, 2H), 7.59 (dd, *J* = 8.2, 7.5 Hz, 1H), 7.27 (dd, *J* = 7.5, 0.7 Hz, 1H), 6.98 (d, *J* = 9.0 Hz, 2H), 6.63 (dd, *J* = 8.2, 0.7 Hz, 1H), 4.03(s, 3H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 163.7, 160.3, 154.4, 139.1, 131,8, 128.0, 114.0, 111.9, 108.3, 55.4, 53.2.

*2-methoxy-4-(4-methoxyphenyl)pyridine – 4-aryl (**3u**):* The compound 4-aryl (**3u**) (new compound) was obtained following the general procedure. It was obtained in 6% yield (0.03 mmol, 6.5 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 8/2 (v/v) to 6/4 (v/v)). Mp: 61 – 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.17 (dd, *J* = 5.4, 0.6 Hz, 1H), 7.58 (d, *J* = 8.9 Hz, 2H), 7.08 (dd, *J* = 5.4, 1.6 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 6.92 (dd, *J* = 1.6, 0.6 Hz, 1H), 3.98 (s, 3H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 164.9, 160.4, 150.7, 147.1, 130.5, 128.1, 115.0, 114.4, 107.7, 55.4, 53.5. HRMS-ESI-TOF: m/z calcd for $C_{13}H_{13}NO_2$ $[M+H]^+$ 216.1024, found 216.1016.

*2-((4-methoxyphenyl)thio)pyridine (**3v**):* The compound (**3v**) (known compound)[100] was obtained following the general procedure. It was obtained in 38% yield (0.189 mmol, 41.0 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9/1 (v/v) to 7/3 (v/v)). Mp: 44 – 46 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.40 (ddd, J = 4.9, 1.9, 0.8 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 2H), 7.42 (ddd, *J* = 8.1, 7.6, 1.9, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.81 – 6.76 (m, 1H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 161.8, 159.7,148.4, 136.2, 135.6, 120.1, 119.4, 118.4, 114.3, 54.4.

*2-(4-methoxyphenyl)quinoline – 2-aryl (**3w**):* The compound 2-aryl (**3w**) (known compound)[101] was obtained following the general procedure. It was obtained in 30% yield (0.150 mmol, 35.4 mg) as a yellow solid after purification over silica gel column

chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 122–123 °C (lit.[101] mp 118–119 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.19-8.12 (m, 4H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.80 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.05 (d, *J* = 8.9 Hz, 2H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 160.8, 156.9, 148.3, 136.6, 132.3, 129.6, 129.5, 128.9, 127.4, 126.9, 125.9, 118.6, 114.2, 55.4.

*4-(4-methoxyphenyl)quinoline – 4-aryl (**3w**):* The compound 4-aryl (**3w**) (known compound)[101] was obtained following the general procedure. It was obtained in 42% yield (0.212 mmol, 50.0 mg) as a yellow solid after purification over silica gel column chromatography (Hexane/EtOAc = from 9.5/0.5 (v/v) to 7/3 (v/v)). Mp: 75–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.92 (d, *J* = 4.4 Hz, 1H), 8.20 – 8.14 (m, 1H), 8.00 – 7.94 (m, 1H), 7.72 (ddd, *J* = 8.4, 1.4, 1.7 Hz, 1H), 7.50 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 4.4 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 159.9, 150.0, 148.7, 148.2, 130.8, 130.3, 129.8, 129.3, 127.0, 126.5, 125.9, 121.3, 114.1, 55.4.

*2-(4-methoxyphenyl)quinoxaline (**3x**):* The compound 2-aryl (**3x**) (known compound)[102] was obtained following the general procedure. It was obtained in 71% yield (0.356 mmol, 84.0 mg) as an orange solid after purification over silica gel column chromatography (Toluene/EtOAc = from 9/1 (v/v)). Mp: 98–100 °C (lit.[102] mp 100–102 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.31 (s, 1H), 8.20 (d, *J* = 8.9 Hz, 2H), 8.16-8.08 (m, 2H), 7.81 – 7.70 (m, 2H), 7.10 (d, *J* = 8.9 Hz, 2H), 3.92 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ_C 161.5, 151.4, 143.1, 142.3, 141.2, 130.2, 129.4, 129.3, 129.1,129.0, 114.6, 55.4.

ASSOCIATED CONTENT

Supporting information: The supporting information is available free of charge on the ACS Publications website at DOI: 101021/acs.joxxxx. Supporting information contains ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra, HRMS–ESI-TOF and all the details of the homemade engineered batch photoreactors.

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