Pyrrolo-imidazo[1,2- a]pyridine Scaffolds through a Sequential Coupling of N -Tosylhydrazones with Imidazopyridines and Reductive Cadogan Annulation, Synthetic Scope, and Application

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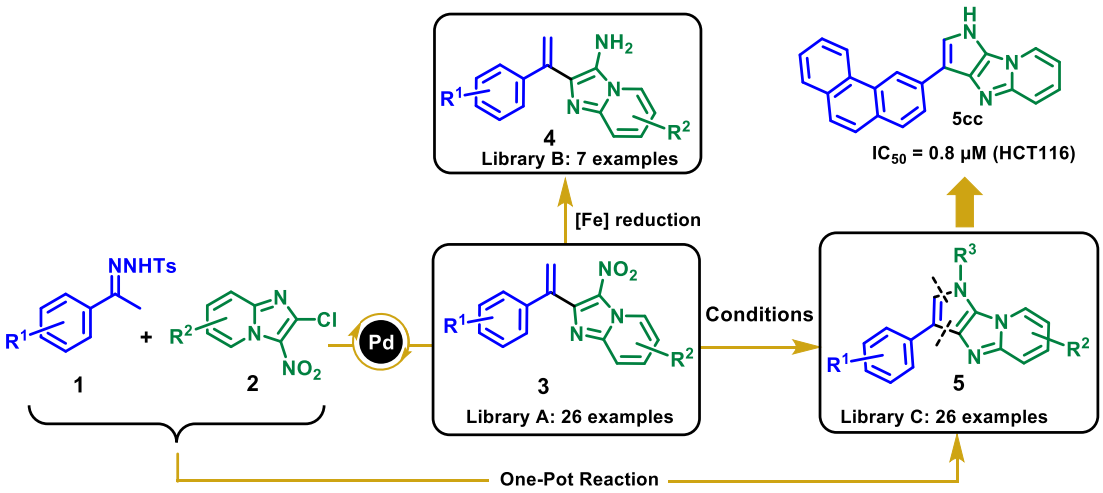


Abstract:

A new strategy for the construction of 3-phenyl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine backbone is described. The reaction starts from the coupling between *N*-tosylhydrazones (NTH) and 2-chloro-3-nitroimidazo[1,2-*a*]pyridines leading to the formation of 3-nitro-2-(arylvinyl)imidazo[1,2-*a*]pyridine derivatives. Optimization of Cadogan-reductive conditions allowed us the conversion of the obtained nitro derivative to a new scaffold of type 3-aryl-1*H*-pyrroloimidazo[1,2-*a*]pyridine. This method provides rapid access to new libraries in the context of diversity-oriented synthesis (DOS) which intends to generate small molecules with a large structure diversity in an efficient manner. Screening of the biological activity of the newly generated compounds leads to the identification of a new hit **5cc** which exhibits good antiproliferative activity in submicromolar range against human colon cancer cell line.

Introduction

Microtubules are essential in various cellular processes, including spindle formation, cellular shape maintenance, and intracellular transport of organelles.[1] Microtubules constitute an attractive target for chemotherapeutic agents to treat cancer.[2] Tubulin binding agents such as natural combretastatin A-4 (CA-4) disrupted efficiently microtubules structures, and present an interesting antivascular activity.[3] CA-4 can isomerize into a thermodynamically more stable

but less active trans isomer.[4] Recently, our efforts in the design of more stable analogs of CA-4 lead us to identify *iso*combretastatin A-4 (*iso*CA-4) with similar antiproliferative activity (Fig. 1).[5] In continuation of our endeavors to have a better understanding of the structure-activity relationship of this series of molecules, we focus on creating compound collections based on privileged scaffolds.

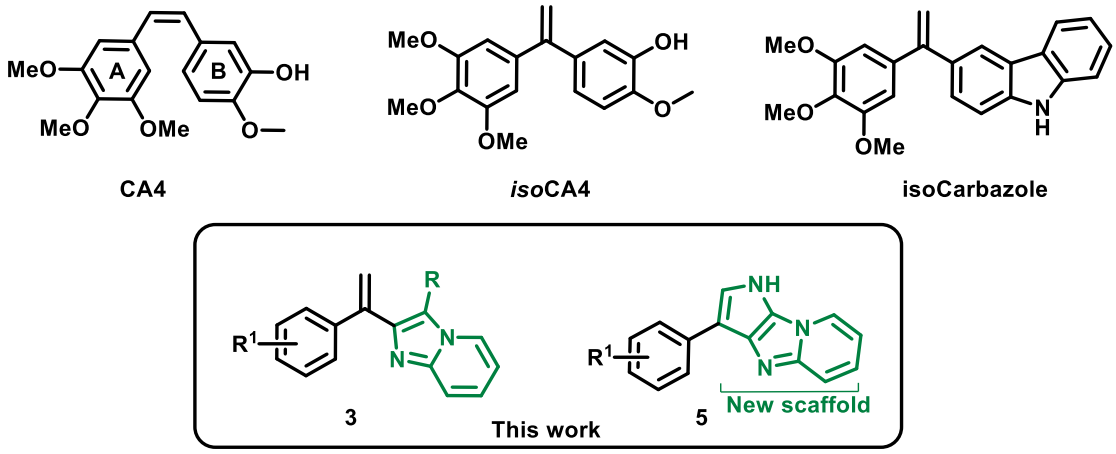
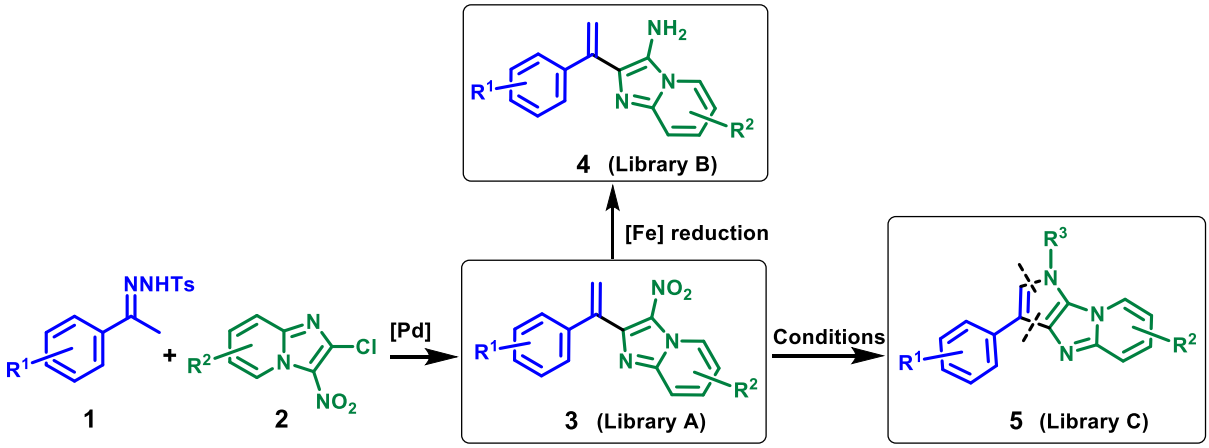


Figure 1. Structures of CA-4, *iso*CA-4, *iso*Carbazole-based tubulin inhibitors and the general structure of target compounds **3** and **5.**

Recently, we identified that the carbazole moiety constitutes a valuable solution to replace the B-ring of *iso*CA-4 with good activity (Fig. 1).[6] Encouraged by these results, we planned to develop a new synthesis which permits us the generation of new scaffolds of biological interests. Imidazo[1,2-*a*]pyridines is an important biologically active moiety, with a growing interest in medicinal chemistry.[7] They have been used as a skeleton in various drugs such as alpidem, olprinone, and zolpidem, and in many lead molecules that are now under human clinical trials.[8] On the other hand, diversity-oriented synthesis (DOS) intends to generate small molecules with a large structure diversity has become a paradigm, providing a larger array of the chemical space in drug discovery. Also, the development of a convergent approach consisting of a complexity-generating reaction followed by cyclization steps and appendage diversity constitutes an emerging area in medicinal chemistry.[9] In the last decade, *N*-tosylhydrazones (NTH) has emerged as a versatile coupling partner for palladium-catalyzed

cross-coupling reactions.[10] From mechanistic point of view, this cross-coupling does not involve the participation of a stoichiometric organometallic species during the catalytic cycle. Thus, the use of NTH as a source of diazo compounds led to the discovery of new C-C[11] and C-heteroatom[12] bond-forming reactions of remarkable synthetic potential. In this context, herein, we report a synthetic method for the synthesis of new libraries of type 2-(1-arylvinyl)imidazo[1,2-*a*]pyridine **3**, and 3-aryl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine **5** (Scheme 1). This method consists of using a convergent reactional sequence: formation of *ortho*-nitro-arenes from NTH and 2-chloro-3-nitroimidazo[1,2-*a*]pyridine followed by a reductive Cadogan cyclization.



Scheme 1. Synthetic strategy for the synthesis of 2-(1-arylvinyl)imidazo[1,2-*a*]pyridine derivatives (library **A** and **B**), and Cadogan cyclization leading to the formation of 3-phenyl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine derivatives (library **C**) .

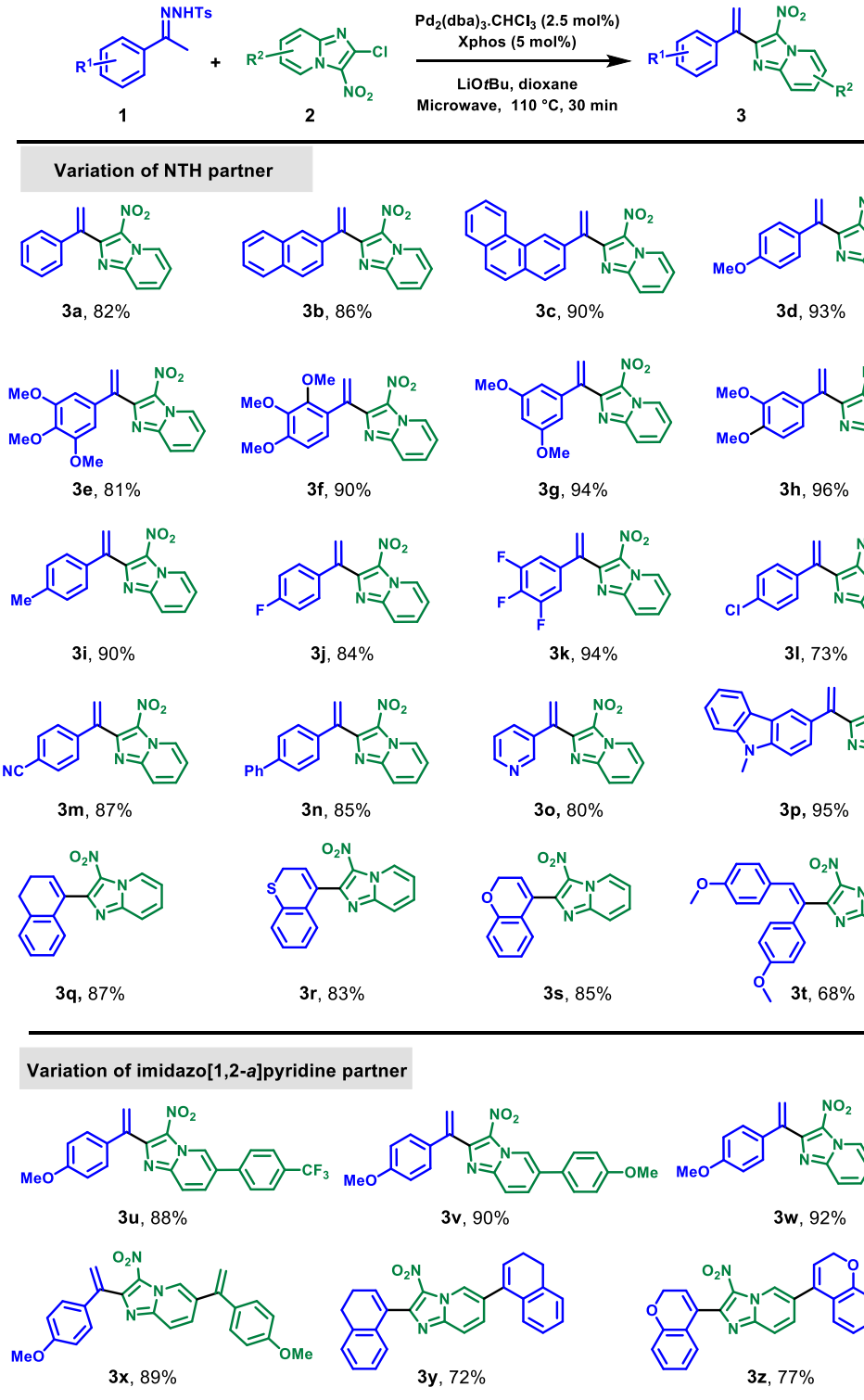
Results and discussion

Initially, 2-chloroimidazo[1,2-*a*]pyridines were synthesized in a two-step procedure from 2-aminopyridine according to Tschitschibabin procedure[13] by condensation of 2-aminopyridine derivatives with chloroacetic acid in the presence of trimethylamine, then the imidazo[1,2-*a*]pyridin-2-ol intermediate was converted to 2-chloroimidazo[1,2-*a*]pyridine in the presence of $POCl_3$. Nitration of this latter compound led to the 2-chloro-3-nitroimidazo[1,2-*a*]pyridine derivatives (**2**) in good yield (For details, see experimental part).

The corresponding 3-nitro-2-(1-arylvinyl)imidazo[1,2-*a*]pyridine derivatives **3** were obtained following Pd-catalyzed coupling between NTH **1** and the corresponding 2-chloro-3-nitroimidazo[1,2-*a*]pyridine **2** in high yield (Scheme 2). The cross-coupling reaction proceeds well either with NTH having ED or EWGs to afford the corresponding 3-nitro-2-(arylvinyl)imidazopyridines **3** in good to high yields (compounds **3a**-**3s**). Also, the coupling tolerates the presence of functional group on the NTH (compounds **3j**, **3l**, and **3m**). Heterocyclic NTHs were also used successfully, and the corresponding compounds (**3o**, **3p**, **3r**, and **3s**) were obtained in good yields. Finally, the modification was obtained with the respect of imidazopyridine partner **2**, and compounds **3u**-**z** were obtained in good yield.

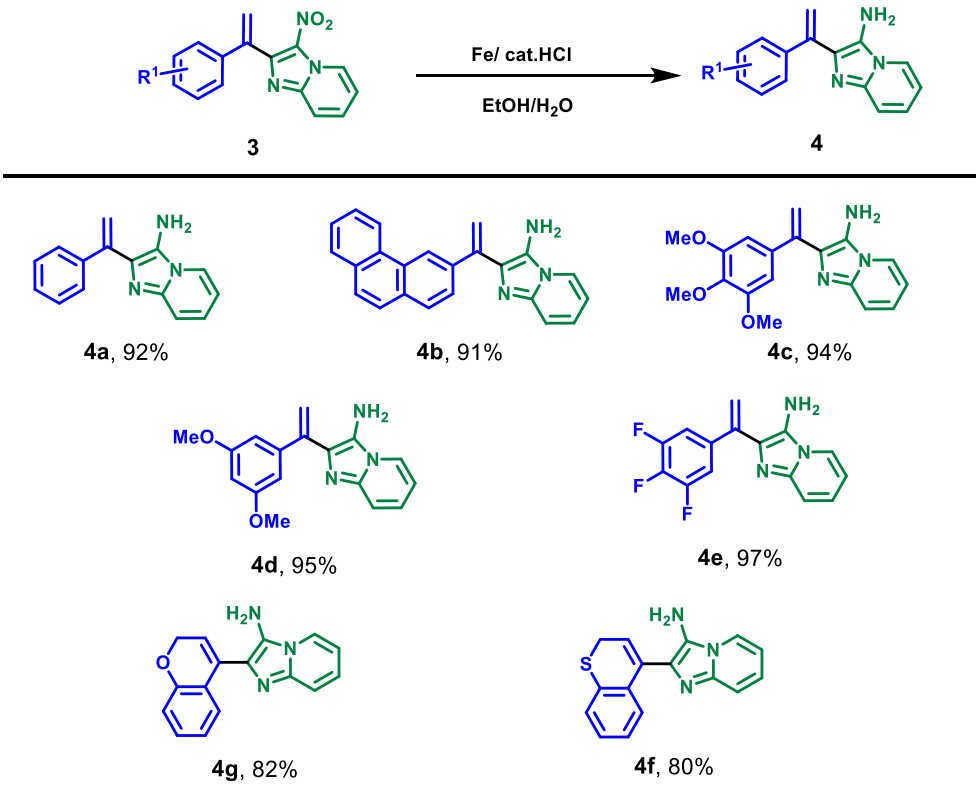
Next, to get more diversity of our compounds, we realized a selective reduction of some nitro compounds **3** to amino derivatives **4**, in the presence of iron and a catalytic amount of HCl, the corresponding products (**4a**-**g**) were obtained in excellent yield (Scheme 3).

Scheme 2. Cross-coupling between *N*-tosylhydrazones **1** and electrophilic partner **2**.[a]



[a] Reaction Conditions: *N*-tosylhydrazone **1** (1 mmol), substrate **2** (1 mmol), $Pd_2dba_3.CHCl_3$ (2.5 mol%), XPhos (5 mol%), LiO*t*Bu (2.2 mmol) in 4 mL of dioxane in a sealed tube, MW 110 °C, 30 min.

Scheme 3. Reduction of 3-nitro-2-(1-arylvinyl)imidazo[1,2-*a*]pyridine derivatives **3** to their corresponding amines **4**.[a]



[a] Iron powder (2 mmol) and concd HCl (ca. 1 µL), nitro-compound (0.2 mmol), EtOH (0.5 mL), water (120 µL), reflux for 90 min.

In order to increase the chemical diversity and generate a new library of compounds, we then took advantage of the presence of nitro group on the (arylvinyl)imidazo[1,2-*a*]pyridine derivatives **3**, to perform a reductive Cadogan cyclization leading to the generation of a novel scaffold of type of 3-aryl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine **5**.

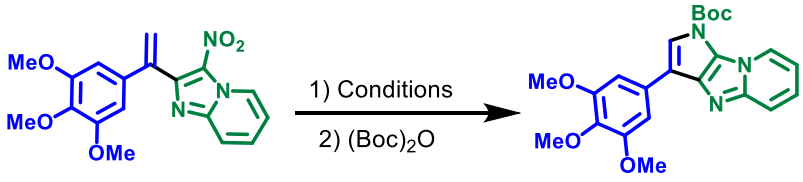
As a model substrate, we started our optimization by performing reductive cyclization on substrate **3e (Table 1)**. As the 3-phenyl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine has the same R_f as the triphenylphosphine oxide generated during the reaction, we protected it in situ by using Boc protection to facilitate the isolation of the desired compound.

Performing the reaction in the presence of PPh_3 in dioxane or in the standard conditions of Cadogan[14] (triethyl phosphite as the solvent) failed to give the desired product (entries 1-4). The presence of nitrogen atom in the structure of the imidazo[1,2-*a*]pyridine derivative seems to slow the reaction in comparison to standard deoxygenation of *ortho*-nitrostyrenes. Recently,

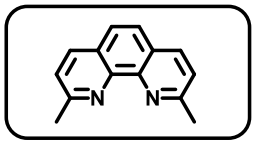
the iron-phenanthroline complex has been reported to catalyze the reductive cyclization of *ortho*-nitrostyrenes into indoles.[15] Accordingly, we tried these optimal conditions on substrate **3e**. As described in Table 1 (entries 5-7), in our hands, only a traces of desired product was observed by using 1 mol % of $Fe(OAc)_2$ and 1 mol % of 4,7-$(MeO)_2$phen and phenylsilane as the reductant in DME (entry 5). Also, no improvement of the conversion was observed by switching from DME solvent to THF or dioxane (entries 6 and 7). Sanz and Arnaiz had developed a molybdenum-catalyzed cyclization of 2-nitrobiphenyls to carbazole.[16] Conducting the reaction on substrate **3** using these reported conditions : $(MoO_2Cl_2(dmf)_2)$ (10 mol%) in the presence of PPh_3 (2.4 equiv) in refluxing toluene or dioxane for 3 h led to a low yield of **5a**, even after the prolongation of the reaction time to 72 h, no improvement of the yield was observed (entry 8). Also, no significant increase in the yield was observed when dioxane was used as the solvent (entry 9). Increasing the amount of reducing agent from 2.4 to 4 equiv. (entry 9 *vs* 10), led to the formation of compound **5e**, after 72 h of heating but only, in a 40% moderate yield.

To reduce the time of this transformation, we performed the reaction in a sealed tube under microwave irradiation at 135 °C (entry 11), to our surprise, the reaction proceeds more rapidly in only 4 h, and the desired product was isolated in a synthetically useful yield of 75%. Performing the reaction in a similar conditions, in a sealed tube but without M.W irradiation (entry 12) led to compound **5e**, in only 45% yield. Although toluene could be used in place of dioxane without attenuating the yield of **5e** (entry 13).

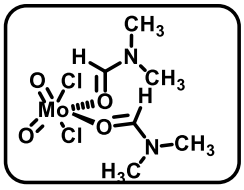
Table 1. Optimization of the reaction conditions for the synthesis of 3-phenyl-1H-pyrrolo-imidazo[1,2-*a*]pyridine [a]



3e **5e**



2,9-Dimethyl-1,10-phenanthroline, DMPHEN
Neocuproine



$MoO_2Cl_2(DMF)_2$

Entry	Catalyst/ ligand	Reducing agents	Solvent	T °C	time	Yield (%)
1		PPh_3	dioxane	160	2h	0
2[b]		PPh_3	diglyme	160	2h	0
3[b]		PPh_3	dioxane	160	48h	0
4[b]		$P(OEt)_3$	$P(OEt)_3$	160	2h	0
5	$Fe(OAc)_2$/ 4,7-$(MeO)_2$phen	$PhSiH_3$	DME	80	12h	trace
6	$Fe(OAc)_2$/ 4,7-$(MeO)_2$phen	$PhSiH_3$	THF	80	12h	trace
7	$Fe(OAc)_2$/ 4,7-$(MeO)_2$phen	$PhSiH_3$	dioxane	110	12h	trace
8[b]	$MoO_2Cl_2(dmf)_2$	PPh_3	toluene	110	72h	20
9[b]	$MoO_2Cl_2(dmf)_2$	PPh_3	dioxane	110	72h	22
10	$MoO_2Cl_2(dmf)_2$	PPh_3	dioxane	110	72h	40
11[c]	$MoO_2Cl_2(dmf)_2$	PPh_3	dioxane	135	4h	75
12	$MoO_2Cl_2(dmf)_2$	PPh_3	dioxane	135	4h	45
13[c]	$MoO_2Cl_2(dmf)_2$	PPh_3	toluene	135	4h	72

[a] Reaction Conditions. **Step 1**: substrate **3a** (0.2 mmol), catalyst (10 mol%), ligand (10 mol%), reducing agent (4 equiv), in 2 mL of solvent were used, in a sealed tube. [b] 2.4 equiv of PPh_3 were used. [c] M.W irradiation was used. **Step 2.** After completion of step 1, $(Boc)_2O$ (0.4 mmol), DMAP (0.04 mmol), TEA (0.6 mmol), were added at rt.

Finally, to prove the importance of M.W irradiation in this transformation, we performed the reaction in a similar condition to entry 11, but without M.W irradiation, in these conditions, compound **5e** was formed in a moderate yield of 45% proving the importance of M.W irradiation.

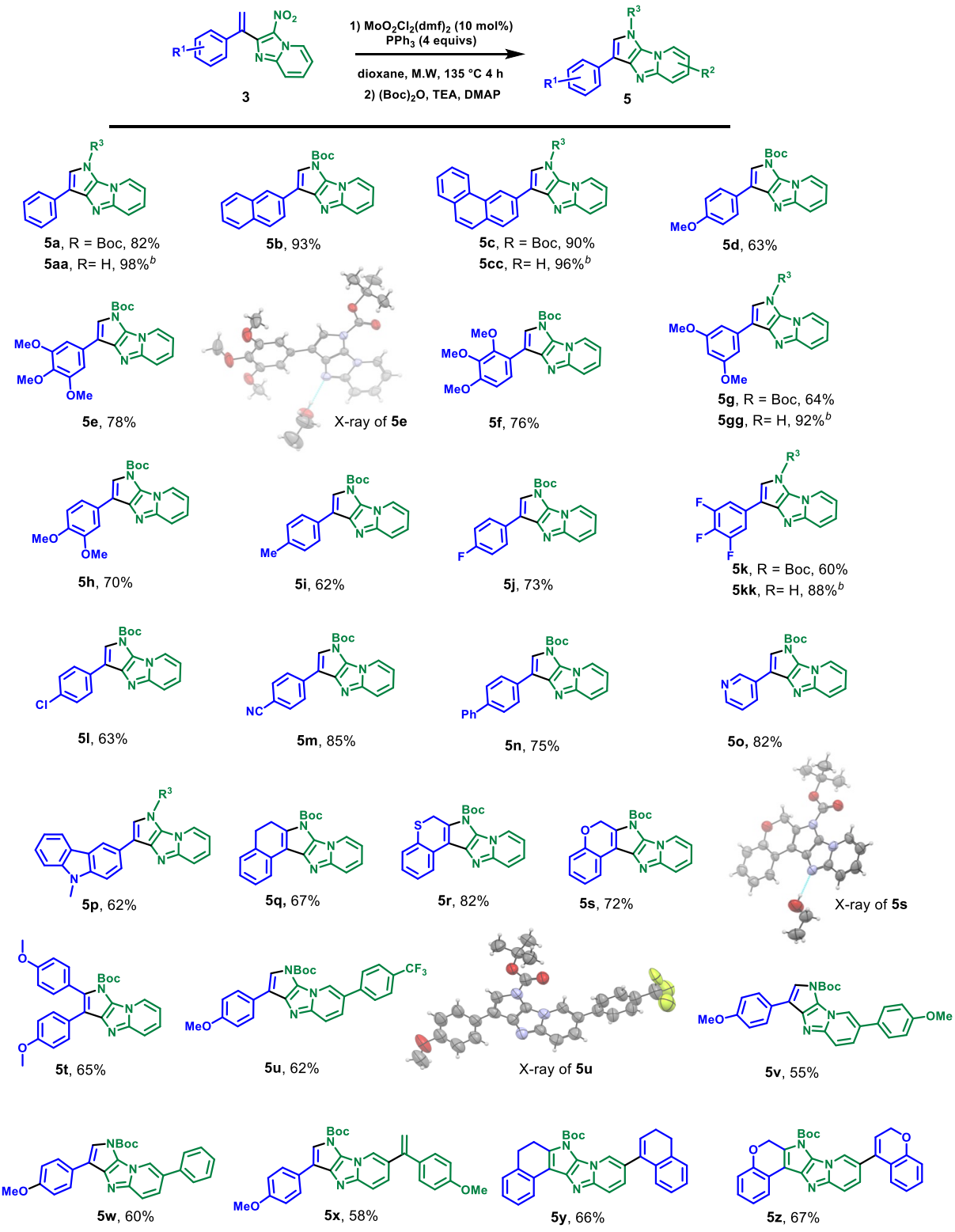
Next, the scope of formation of 3-phenyl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine derivatives with different substituents was evaluated under the optimized conditions (scheme 4).

The cyclization of the nitro derivatives bearing substituents on the benzene ring could be varied and both EDG (MeO, Me), and EWG (F, CN, Cl), all proceeded efficiently to lead, the corresponding products in good to excellent yield. The structure of compounds **5e**, **5s**, and **5u** was established by X-ray diffraction.[17]

It is noteworthy that phenyl (**5a**), naphtyl (**5b**), phenantryl (**5c**) or heterocyclic derivatives (**5o**, **5p**, **5r** and **5s**) were also identified as suitable substrates for the reaction, delivering the products in good yield. Next, the scope of the reaction was evaluated by modifying the imidazo[1,2-*a*]pyridine partner. The reaction proceeds also with trisubstituted alkenes (**3q**-**t**, **3y** and **3z**) under our similar conditions to give 2,3 disubstituted pyrrolo-imidazo[1,2-*a*]pyridine derivatives (**5q-t, 5y** and **5z**). A series of substituents, including phenyl, 4-methoxyphenyl or 4-(trifluoromethyl)phenyl, on position 7 of imidazo[1,2-*a*]pyridine were evaluated, and the corresponding products were obtained in a moderate to good yield (compounds **5u**-**z**).

In the medicinal chemistry context, it would be interesting to dispose of the free nitrogen form of the heterocycle. To this end, we realized the deprotection of some compound using mild conditions, by heating the protected form of the pyrrolo-imidazo[1,2-*a*]pyridine in a mixture of MeOH/H_2O, and catalytic amount of trifluoroacetic acid under M.W irradiation for 30 minutes. Under these conditions, the desired compounds were obtained in a nearly quantitative yield (Scheme 4, compounds **5aa**, **5cc**, **5gg**, and **5kk**).

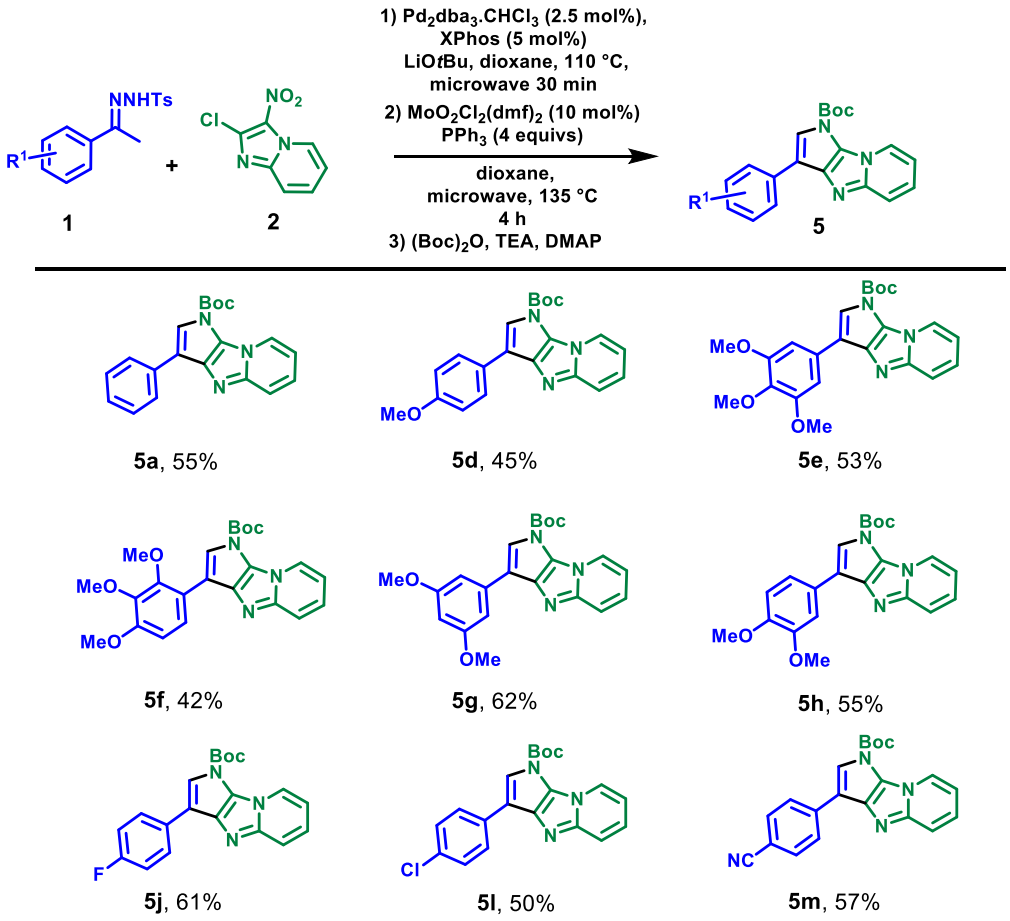
Scheme 4. Reductive cyclization of nitro-2-(1-phenylvinyl)imidazo[1,2-*a*]pyridine **3** to 3-phenyl-1H-pyrrolo-imidazo[1,2-*a*]pyridine derivatives **5**.[a]



[a]Reaction Conditions: Step 1. substrate **3** (0.5 mmol), $MoO_2Cl_2(dmf)_2$ (10 mol%) PPh_3 (4 equiv), in 3 mL of dioxane, in a sealed tube. MW 135 °C, 4 h. Step 2. After completion of step 1, $(Boc)_2O$ (0.65 mmol), DMAP (0.1 mmol), TEA (1.5 mmol), were added at rt. [b] Deprotection step: protected heterocycle (0.5 mmol) in MeOH/H_2O (1/3), TFA (ca. 5 µL) was heated under MW at 110 °C for 30 min.

Finally, we wished to examine the possibility to realize this transformation in a one-pot fashion, starting from NTH **1** and 2-chloroimidazo[1,2-*a*]pyridines **2**. As presented in Scheme 5, many compounds were successfully obtained, with an average of 50% yield after 3 sequential steps. This represents an average of ~ 80% for each step of this transformation.

Scheme 5. Substrate scope of the one-pot cross-coupling between *N*-tosylhydrazones **1** and 2-chloro-3-nitroimidazo[1,2-*a*]pyridine **2**.[a]



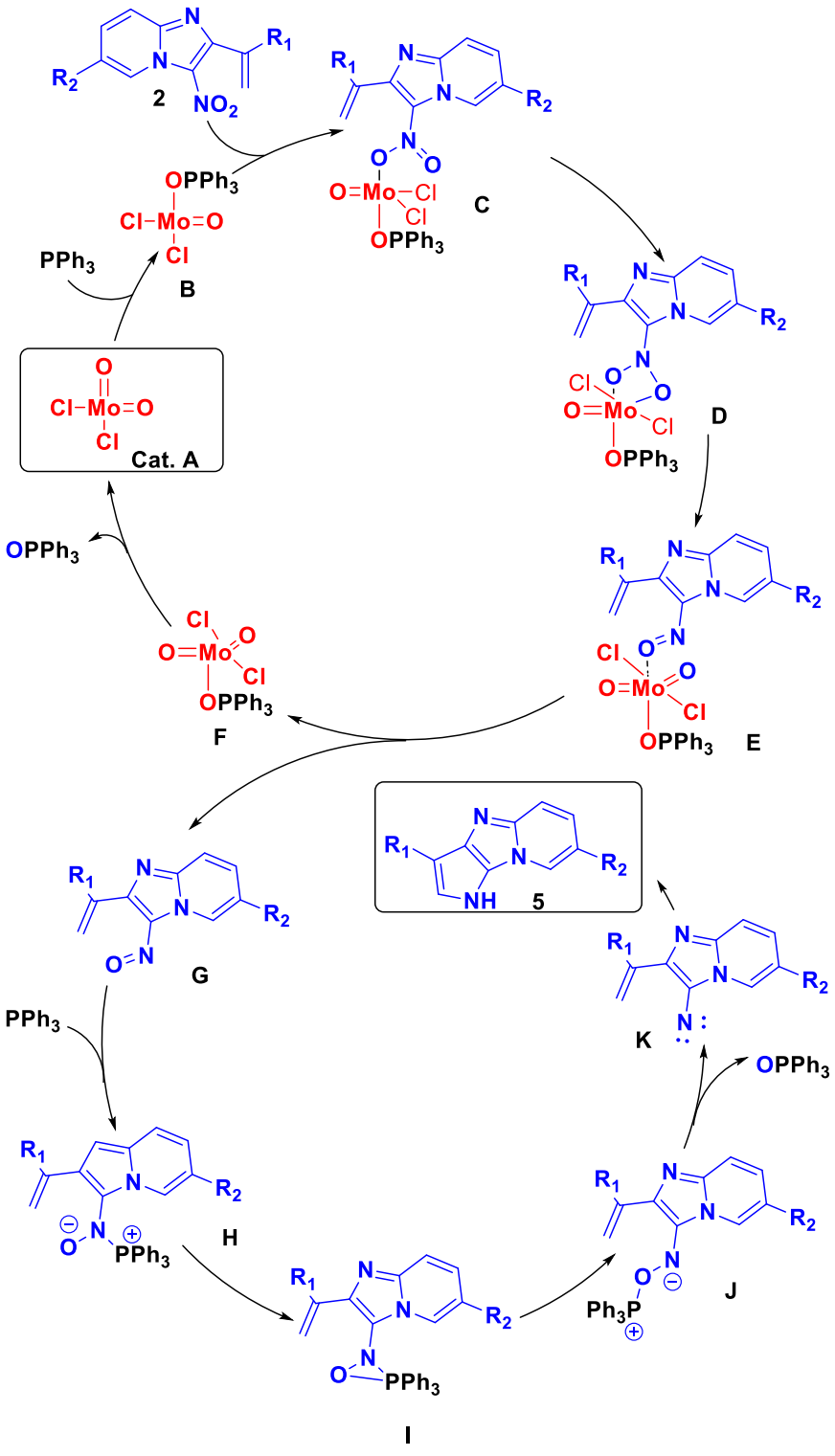
[a] Reaction Conditions: Step 1. *N*-tosylhydrazone **1** (1 mmol), substrate **2** (1 mmol), $Pd_2dba_3.CHCl_3$ (2.5 mol%), XPhos (5 mol%), LiO*t*Bu (2.2 mmol) in 4 mL of dioxane in a sealed tube, MW 110 °C, 30 min. Then $MoO_2Cl_2(dmf)_2$ (10 mol%), PPh_3 (4 equiv), were added, and the mixture was irradiated at 135 °C for 4 h. Step 2. After completion of step 1, $(Boc)_2O$

(1.3 mmol), DMAP (0.2 mmol), TEA (mmol), were added and the mixture was stirred at rt for 2 h.

Mechanism

On the basis of the work of Faza *et al*,[18] a mechanism for Mo-catalyzed reductive Cadogan-type reaction of 3-nitro-2-(1-arylvinyl)imidazo[1,2-*a*]pyridines in the presence of PPh_3 to give 3-aryl-1H-pyrroloimidazo[1,2-*a*]pyridines is proposed in Scheme 6.

The reduction of Mo(VI) catalyst **A** will take place in the presence of the PPh_3 leading to the formation of Mo(IV) complex **B**. Then the complexation of 2-nitroimidazopyridine **2** to **B** lead to the formation of complex **C**. Then, the octahedral complex **D** is formed after chelation with the nitro ligand. This complex can evolve toward complex **E** in which the initial nitro group loses an oxygen atom. Complex **E** can then evolve through cleaving of nitrosaromatic ligand **G** yielding to complex **F**. Finally, the leaving of the $OPPh_3$ ligand from complex **F** recovers the initial catalyst **A** which can restart a new cycle. A second equivalent of PPh_3 attacks the nitrogen atom of **G** leading to complex **H**, which can evolve to oxazaphosphiridine intermediate **I**. Than the nitrogen-phosphore bond in **I** is cleaved leading to the formation of intermediate **J** which thereafter lead to the nitrene derivative **K** accompanied with the formation of $OPPh_3$. Finally, subsequent cyclization of the resulting intermediate nitrene **K** leads to the formation of pyrroloimidazo[1,2-*a*]pyridine derivative **5.**



Scheme 6. Mo-catalyzed reductive Cadogan-type reaction of 3-nitro-2-(1-arylvinyl)imidazo[1,2-a]pyridines to give 3-aryl-1H-pyrroloimidazo[1,2-*a*]pyridines

Biological studies.

Screening assay. The analogues generated in this work were initially screened using human colon cancer cell line (HCT116) at 10^{-5} M concentration by CellTiter-Glo® luminescent cell viability assay, which is a homogeneous method of determining the number of viable cells in culture based on quantitation of the ATP present (an indicator of metabolically active cells). The amount of ATP is directly proportional to the number of cells present in culture. The compounds inhibited HCT116 cell proliferation with varying ability as shown in Figure 2. Compounds which were not active on the cell proliferation were excluded from the Figure 2. Of the compounds evaluated, 4 compounds (**3e**, **3g**, **3k**, and **5cc**) showed more than 50% inhibition of HCT116 cell proliferation at 10^{-5} M concentration (Figure 2).

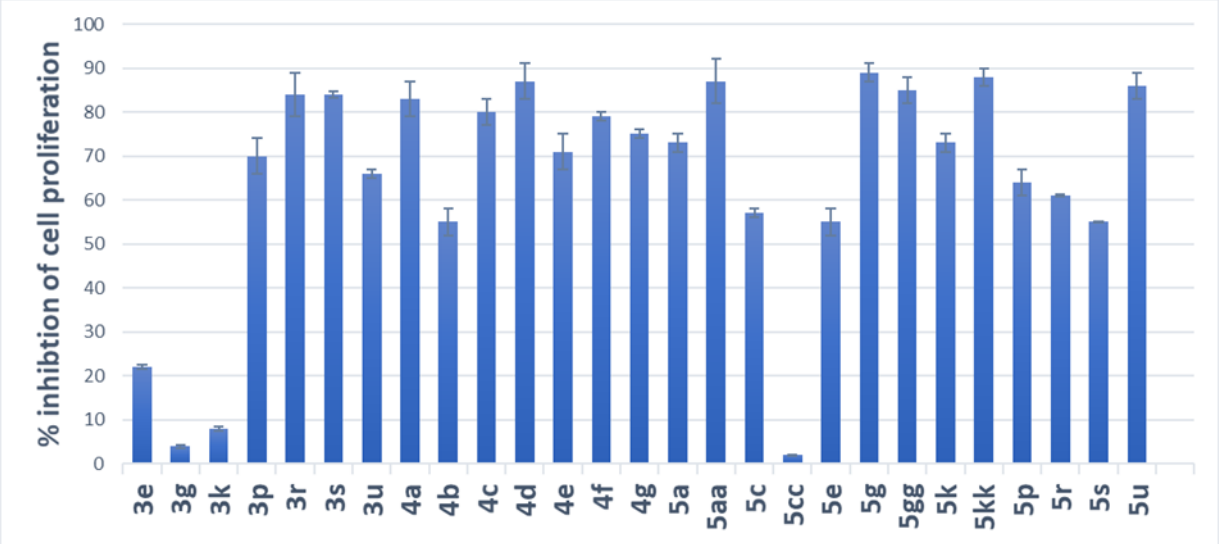
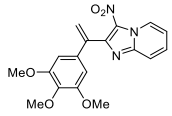
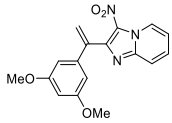
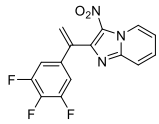
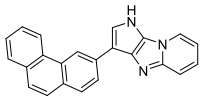
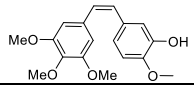


Figure 2. Screening of generated analogues in HCT116 cells. The inhibition of cell proliferation was plotted for each of the analogue at 10^{-5} M concentration in HCT116 cells. Three sets of experiments were carried out. Error bars represent standard deviation.

To find out the most active compound against human colon cancer cell line, the IC_{50} (half-maximal inhibitory concentration) of these active compounds was determined in HCT116 cells in comparison with natural combretastatin A-4 (CA-4).

The analysis of these results show that the replacement of the methoxy group on the phenyl ring by a fluorine atom led to an increase of the antiproliferative activity (compounds **3e** vs **3k**). Among tested compounds (Table 2), the best antiproliferative activity was obtained with compound **5cc** (IC_{50} = 0.8 μM) having a phenanthren-3-yl group instead of the cycle A of CA-4, and pyrroloimidazo[1,2-*a*]pyridine ring in lieu of cycle B. As compound **5cc** did not have a *Z* double-bond in its skeleton, it should escape to the risk of isomerization which is the Achilles tendon of natural CA-4. This study opens the door to the development of a new structure-activity relationship around this compound to allow the discovery of a new lead-compound.

Table 2. Cytotoxic activity of selected derivatives against HCT116 cells[a]

Compound no.	structure	IC_{50} (µM)[b]
3e		13.7 ± 1.4
3g		2.2 ± 1.3
3k		2.1 ± 0.2
5cc		0.8 ± 0.002
CA-4		0.01 ± 0.001[c]

[a] HCT-116 human colon carcinoma cells. [b] Compound concentration required to decrease cell growth by 50%; values represent the average SD of three experiments. [c] The IC_{50} value for CA-4 was determined in this study.

Conclusion

In summary, this work reports a Pd-catalyzed cross-coupling reaction between NTH and 2-chloroimidazo[1,2-*a*]pyridines partners leading to the formation of nitro-2-(1-phenylvinyl)imidazopyridine derivatives, subsequent optimization of Codagan-reductive

cyclization allowed the formation of 3-phenyl-1*H*-pyrrolo-imidazo[1,2-*a*]pyridine derivatives which represents a new scaffold in medicinal chemistry. This methodology is suitable for diversity-oriented synthesis technology given the fact that starting from the same building block, diversity can be obtained easily by application of late-stage modification process. Among evaluated derivatives, compound **5cc** exhibited the highest cytotoxic activity (IC_{50} = 0.8 μM) against human colon cancer cell line.

EXPERIMENTAL SECTION

General Methods. Solvent peaks were used as reference values, with $CDCl_3$ at 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR. Chemical shifts δ are given in ppm, and the following abbreviations are used: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), multiplet (m) and broad singlet (bs). Reaction courses and product mixtures were routinely monitored by TLC on silica gel, and compounds were visualized with under a UVP Mineralight UVGL-58 lamp (254 nm) and with phosphomolybdic acid/Δ, anisaldehyde/Δ, or vanillin/Δ. Flash chromatography was performed using silica gel 60 (40–63 mm, 230–400 mesh) at medium pressure (200 mbar). Dioxane, dichloromethane, cyclohexane and tetrahydrofuran were dried using the procedures described in D. Perrin Purification of Laboratory Chemicals.[19] Organic extracts were, in general, dried over $MgSO_4$ or Na_2SO_4. High-resolution mass spectra were recorded with the aid of a MicrOTOF-Q II. All products reported showed ^{1}H and ^{13}C NMR spectra in agreement with the assigned structures.

Microwave Irradiation Experiments.

The Microwave reactor used was a Biotage microwave reaction Kit, 2-5 mL; manufacturer number: 351521. All reactions were conducted in a sealed reaction vessel, and the reaction temperature was monitored by external surface sensor.

General procedure for preparation of hydrazone[20]

p-toluenesulphonylhydrazide (930 mg, 5 mmol) was placed in a round-bottom boiling flask equipped with reflux condenser in a 10 mL of dry methanol, the ketone (5 mmol) was added slowly and the mixture was heated in an oil bath, at 60 °C. Within 5-60 min the *N*-tosylhydrazone began to precipitate. The mixture was cooled to 0 °C and the product was collected on a Büchner funnel, washed by petroleum ether than was dried *in vacuo* to afford the pure product.

*4-Methyl-N'-(1-phenylethylidene)benzenesulfonohydrazide (**1a**).*[21] white solid (1.34 g, 95% yield); mp 148-151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.11 (s, 1H), 7.94 (d, J = 8.3 Hz, 2H), 7.64 (dd, J_1 = 6.6 Hz, J_2 = 2.9 Hz, 2H), 7.35-7.30 (m, 5H), 2.41 (s, 3H), 2.17 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 152.8, 144.2, 137.4, 135.6, 129.7 (2CH), 129.6, 128.4 (2CH), 128.2 (2CH), 126.4 (2CH), 21.7 (CH_3), 13.6 (CH_3).

*4-Methyl-N'-(1-(naphthalen-2-yl)ethylidene)benzenesulfonohydrazide (**1b**).*[22] white solid (1.52 g, 90% yield); mp 260-268 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.18 (s, 1H), 8.02-7.94 (m, 4H), 7.86-7.79 (m, 3H), 7.52-7.49 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 2.42 (s, 3H), 2.30 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 152.4, 144.2, 135.5, 134.7, 133.8, 132.9, 129.6 (2CH), 128.5, 128.2 (2CH), 128.0, 127.6, 126.9, 126.4, 126.2, 123.5, 21.6, 13.3.

*4-Methyl-N'-(1-(phenanthren-3-yl)ethylidene)benzenesulfonohydrazide (**1c**).* white solid (1.9 g, 98%); mp 150-160 °C; IR (film, cm^{-1}): 3214, 1402, 1335, 1305, 1166, 1060, 915, 863, 842, 814, 752, 734, 706, 693, 662; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.89 (s, 1H), 8.67 (d, J = 8.1 Hz, 1H), 8.04 (d, J = 8.1 Hz, 2H), 7.99-7.82 (m, 4H), 7.79-7.63 (m, 4H), 7.38 (d, J = 8.3 Hz, 2H), 2.44 (s, 3H), 2.37 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 152.7, 144.2, 135.5, 135.2, 132.7, 132.2, 130.4, 129.8, 129.6 (2CH), 128.7, 128.6, 128.3 (2CH), 128.0, 126.8, 126.8, 126.4, 124.3, 122.5, 120.8, 21.6, 13.6; HRMS (ESI): for $C_{23}H_{21}N_2O_2S$ $(M + H)^+$: m/z calcd. 389.1324, found 389.1317.

N'-(1-(4-Methoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1d).***[21] white solid (1.52 g, 96%); mp 168-170 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.92 (d, J = 8.0 Hz, 2H), 7.74 (s, 1H), 7.60 (d, J = 8.6 Hz, 2H), 7.31 (d, J = 7.9 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 3.81 (s, 3H), 2.41 (s, 3H), 2.12 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 161.0, 152.8, 144.2, 135.7, 130.0, 129.3 (2CH), 128.3 (2CH), 127.9 (2CH), 113.8 (2CH), 55.4 (OCH_3), 21.7 (CH_3), 13.4 (CH_3).

4-Methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide ***(1e).***[5a] white solid (1.77 g, 94%); mp 167-168 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.92 (d, J = 8.2 Hz, 2H), 7.76 (s, 1H), 7.30 (d, J = 8.2 Hz, 2H), 6.86 (s, 2H), 3.86 (s, 6H), 3.85 (s, 3H), 2.41 (s, 3H), 2.14 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 153.1, 152.5, 144.4, 135.6, 132.9, 129.6 (2CH), 128.4 (2CH), 106.1, 104.1 (2CH), 103.7, 61.0 (OCH_3), 56.3 ($2OCH_3$), 21.7 (CH_3), 13.6 (CH_3).

4-Methyl-N'-(1-(2,3,4-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide ***(1f).*** white solid (1.74 g, 92%); mp 163-165 °C; IR (film, cm^{-1}): 1597, 1494, 1465, 1414, 1340, 1306, 1291, 1217, 1168, 1094, 667; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.84 (d, J = 8.3 Hz, 2H), 7.67 (s, 1H), 7.33 (d, J = 7.8 Hz, 2H), 6.75-6.64 (m, 2H), 3.88 (s, 6H), 3.56 (s, 3H), 2.45 (s, 3H), 2.18 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 155.0, 152.7, 143.7, 135.8, 129.4 (2CH), 127.9 (2CH), 124.0, 122.2, 120.2, 108.5, 107.2, 61.3, 61.1, 56.2, 25.0, 21.6; HRMS (ESI): for $C_{18}H_{23}N_2O_5S$ $(M + H)^+$: m/z calcd. 379.1328, found 379.1324

N'-(1-(3,5-Dimethoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1g).***[12a] white solid (1.7 g, 90%); mp 230-232 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.95 (s, 1H), 7.92 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 2.1 Hz, 2H), 6.52-6.32 (m, 1H), 3.78 (s, 6H), 2.40 (s, 3H), 2.11 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 160.7 (2C), 152.5, 144.3, 139.4, 135.6, 129.7 (2CH), 128.3 (2CH), 128.0, 104.8 (2CH), 101.8, 55.5 (OCH_3), 21.7 (CH_3), 13.7 (CH_3).

N'-(1-(3,4-Dimethoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1h).***[21] white solid (1.75 g, 93%); mp 220-222 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.94 (d, J = 8.1 Hz, 2H), 7.67 (s, 1H), 7.38-7.25 (m, 3H), 7.15 (ddd, J_1 = 8.4 Hz, J_2 = 2.1 Hz, J_3 = 0.8 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 2.43 (s, 3H), 2.15 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 152.6, 150.6, 148.8, 144.1, 135.5, 130.1, 129.5 (2CH), 128.2 (2CH), 119.6, 110.3, 108.9, 55.9, 55.8, 21.6, 13.2.

4-Methyl-N'-(1-(p-tolyl)ethylidene)benzenesulfonohydrazide ***(1i).***[21] white solid (1.36 g, 90%); mp 195-198 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.93 (d, J = 8.0 Hz, 2H), 7.87 (s, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 2.41 (s, 3H), 2.34 (s, 3H), 2.14 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 152.8 (C), 144.2 (C), 139.8 (C), 135.7 (C), 134.7 (C), 129.7 (CH), 129.1 (CH), 128.3 (CH), 126.3 (CH), 21.7 (CH_3), 21.4 (CH_3), 13.5 (CH_3).

N'-(1-(4-Fluorophenyl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1j).***[21] white solid (1.36 g, 89%); mp 185-188 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.94 (d, J = 8.0 Hz, 2H), 7.79 (s, 1H), 7.65 (dd, J_1 = 8.6 Hz, J_2 = 5.4 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.04 (t, J = 8.5 Hz, 2H), 2.44 (s, 3H), 2.16 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 163.8 (d, $J_{C\text{-}F}$ = 250.0 Hz), 151.7 (C), 144.4 (C), 135.6 (C), 133.6 (d, $J_{C\text{-}F}$ = 2.4 Hz), 129.8 (2CH), 128.4 (CH), 128.3 (3CH), 115.6, 115.3, 21.7 (CH_3), 13.5 (CH_3).

4-Methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide ***(1k).***[2b] white solid (1.45 g, 85%); mp 188-190 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.92 (d, J = 8.2 Hz, 2H), 7.74 (s, 1H), 7.31 (d, J = 8.1 Hz, 2H), 6.86 (s, 2H), 3.86 (s, 6H), 3.85 (s, 3H), 2.41 (s, 3H), 2.14 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm) 152.9 (2C), 152.5 (C), 144.2 (C), 139.6 (C), 135.4 (C), 132.8 (C), 129.5 (2CH), 128.2 (2CH), 103.8 (2CH), 60.9 (CH_3), 56.1 (2CH_3), 21.6 (CH_3), 13.6 (CH_3). HRMS (ESI) $(M + H)^+$ *m/*z calcd for $C_{18}H_{23}N_2O_5S$ 379.1322 found 379.1325.

N'-(1-(4-chlorophenyl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1l).***[21] white solid (1.58 g, 98%); mp 155-156 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.01 (s, 1H), 7.91 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.31 (t, J = 7.6 Hz, 4H), 2.41 (s, 3H), 2.14 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 151.4 (C), 144.4 (C), 135.9 (C), 135.8 (C), 135.5 (C), 129.8 (2CH), 128.7 (2CH), 128.2 (2CH), 127.7 (2CH), 21.7 (CH_3), 13.4 (CH_3).

N'-(1-(4-cyanophenyl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1m)***.[21] white solid (1.34 g, 86%); mp 221-223 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.10 (s, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.74 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 2.42 (s, 3H), 2.17 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 149.9 (C), 144.7 (C), 141.5 (C), 135.3 (C), 132.3 (2CH), 129.9 (2CH), 128.2 (2CH), 126.9 (2CH), 118.6 (C), 113.1 (C), 21.8 (CH_3), 13.3 (CH_3).

N'-(1-([1,1'-biphenyl]-4-yl)ethylidene)-4-methylbenzenesulfonohydrazide ***(1n).***[23] white solid (1.63 g, 90%); mp 194-196 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.85 (d, J = 8.0 Hz, 2H), 7.74-7.66 (m, 6H), 7.53-7.30 (m, 5H), 2.37 (s, 3H), 2.22 (s, 3H); ^{13}C{1H} NMR (75 MHz, DMSO-d_6) δ 152.6, 143.3, 140.9, 139.3, 136.4, 136.3, 129.4 (2CH), 128.9 (2CH), 127.7, 127.5 (2CH), 126.5 (6CH), 21.0, 14.2.

4-Methyl-N'-(1-(pyridin-3-yl)ethylidene)benzenesulfonohydrazide ***(1o).***[24] white solid (1.33 g, 92%); mp 198-200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.86 (d, J = 2.3 Hz, 1H), 8.59 (dd, J_1 = 4.8 Hz, J_2 = 1.5 Hz, 1H), 8.32 (s, 1H), 8.01-7.88 (m, 3H), 7.41-7.28 (m, 3H), 2.43 (s, 3H), 2.21 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 150.2, 149.7, 147.5, 144.4, 135.2, 133.6, 133.0, 129.7 (2CH), 128.1 (2CH), 123.2, 21.6, 13.2.

4-Methyl-N'-(1-(9-methyl-9H-carbazol-3-yl)ethylidene)-benzenesulfonohydrazide ***(1p).***[2c] White solid (2.95 mmol, 59%); mp: 177−178°C;^{1}H NMR (300 MHz,$CDCl_3$) δ (ppm) 8.32 (d, J = 1.2 Hz, 1H), 8.10 (d, J = 7.7 Hz, 1H),8.03 (d, J = 8.3 Hz, 2H), 7.89 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2H), 7.51(t, J = 7.6 Hz, 1H), 7.42 (s, 1H), 7.40-7.30 (m, 4H), 7.27 (d, J = 7.7Hz, 1H),

3.83 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H);^{13}C{1H} NMR (75MHz, $CDCl_3$) δ 154.1, 144.2, 141.9, 141.6,135.8, 129.7 (2CH), 128.5, 128.4 (2CH), 126.2, 124.4, 123.0, 122.6, 120.4, 119.5, 118.8, 108.9, 108.4, 29.3, 21.7, 13.9.

(E)-N'-(3,4-dihydronaphthalen-1(2H)-ylidene)-4-methylbenzenesulfonohydrazide ***(1q).***[21] white solid (1.38 g, 88%); mp 178-180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.05-7.93 (m, 3H), 7.83 (s, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.29-7.16 (m, 2H), 7.10 (dd, J_1 = 7.3, J_2 = 1.7 Hz, 1H), 2.76-2.69 (m, 2H), 2.49 (t, J = 6.5 Hz, 2H), 2.43 (s, 3H), 1.90 (p, J = 6.5 Hz, 2H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 152.4, 144.1, 139.7, 135.5, 131.6, 129.6 (2CH), 129.5, 128.3, 128.1 (2CH), 126.4, 125.0, 29.3, 25.4, 21.6, 21.4.

(E)-4-methyl-N'-(thiochroman-4-ylidene)benzenesulfonohydrazide ***(1r).*** white solid (1.48 g, 89%); mp 199-201 °C; IR (film, cm^{-1}): 3207, 1403, 1343, 1316, 1167, 1089, 998, 917, 761, 707, 681, 664; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.08 (s, 1H), 8.01 (dd, J_1 = 7.9, J_2 = 1.2 Hz, 1H), 7.94 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 4.2 Hz, 2H), 7.12 (dt, J_1 = 8.3, J_2 = 4.3 Hz, 1H), 3.01 – 2.91 (m, 2H), 2.86 (dd, J_1 = 7.1, J_2 = 5.3 Hz, 2H), 2.43 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 150.1, 144.3, 136.2, 135.28, 130.8, 129.7 (2CH), 129.4, 128.2, 128.1 (2CH), 126.9, 125.6, 27.9, 25.7, 21.6; HRMS (ESI): for $C_{16}H_{17}N_2O_2S_2$ $(M + H)^+$: m/z calcd. 333.0731, found 333.0729.

(E)-N'-(chroman-4-ylidene)-4-methylbenzenesulfonohydrazide ***(1s).***[21] white solid (1.36 g, 86%); mp 178-180°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.17 (s, 1H), 7.98-7.88 (m, 3H), 7.35 (d, J = 8.0 Hz, 2H), 7.25 (ddd, J_1 = 8.9 Hz, J_2 = 7.1 Hz, J_3 = 1.8 Hz, 1H), 6.97-6.92 (m, 1H), 6.86 (dd, J_1 = 8.3, J_2 = 1.1 Hz, 1H), 4.22 (t, J = 6.2 Hz, 2H), 2.72 (t, J = 6.2 Hz, 2H), 2.44 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 157.2, 148.0, 144.3, 135.3, 131.5, 129.6 (2CH), 128.1 (2CH), 125.0, 121.5, 119.7, 117.5, 64.5, 25.2, 21.6.

General procedure for the synthesis of chloroimidazo[1,2-*a*]pyridine derivatives.[25]

In a 100 mL round bottom flask containing a solution of chloroacetic acid (3.67 g, 38.8 mmol) in water (6 mL), triethylamine (6.12 mL, 44 mmol) was added dropwise. After stirring for a few minutes, 2-aminopyridine or 2-amino-5-bromopyridine (46 mmol) was added and the mixture was heated to reflux in an oil bath for 5 h. The reaction mixture was allowed to cool, ethanol (10 mL) was added, stirred at 5 °C for 2 h to obtain precipitates. These precipitates were collected and dissolved in toluene (25 mL) followed by addition of phosphorous oxychloride (9.7 mL, 104 mmol) at reflux. After 16 h reaction mixture was cooled to room temperature, diluted with cold water (100 mL) and stirred for 15 min. Aqueous layer was separated and neutralized with 10% aqueous NaOH (aq) and the precipitates obtained were filtered and dissolved in dichloromethane. The organic layer was washed with brine, dried over anhydrous $MgSO_4$ and concentrated under vacuum to afford a brown powder which was purified using column chromatography on silica gel using cyclohexane: ethyl acetate (90:10) as eluent to yield the corresponding chloroimidazo[1,2-*a*]pyridine derivatives.

The isolated chloroimidazo[1,2-*a*]pyridine derivatives in the last step (40 mmol) was added to concentrated sulfuric acid solution (60 mL) under ice bath at 5 °C followed by addition of nitric acid (6 mL) dropwise. After addition, reaction was allowed to stir at room temperature for 3 h. The reaction mixture was poured onto crushed ice, and precipitates were filtered by vacuum filtration and dissolved in dichloromethane. This organic layer was dried on anhydrous sodium sulphate and concentrated under vacuum to yield crude product which was purified by column chromatography on silica gel using cyclohexane: ethyl acetate (8:2) as eluent to give **2a** or **2b**.

*2-Chloro-3-nitroimidazo[1,2-a]pyridine (**2a**)*.[25] Yellow solid (6.4 g, 70%); mp 171-173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.42 (d, J = 7.0 Hz, 1H), 7.72 (dt, J_1 = 15.8 Hz, J_2 = 8.9 Hz, 2H), 7.33 (t, J = 6.9 Hz, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 143.5, 140.2, 131.6, 128.6, 128.0, 117.9, 117.1.9

*6-Bromo-2-chloro-3-nitroimidazo[1,2-a]pyridine (**2b**)*. Yellow solid (7.1 g, 65%); mp 168-170 °C; IR (film, cm^{-1}): 3140, 1507, 1470, 1440, 1414, 1358, 1341, 1318, 1221, 1208, 814; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.58 (s, 1H), 7.79-7.78 (m, 1H), 7.65 (d, J = 9.4 Hz, 1H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 141.8, 135.0, 128.0, 122.1, 121.7, 118.4, 112.4; HRMS (ESI): for $C_7H_4BrClN_3O_2$ $(M + H)^+$: m/z calcd. 275.9175, found 275.918.

General procedure for the synthesis of substituted chloroimidazo[1,2-a]pyridine derivatives

A 10 mL sealed tube under argon atmosphere was charged with 6-bromo-2-chloro-3-nitroimidazo[1,2-a]pyridine (1.0 mmol, 1.0 equiv.), corresponding boronic acid (1.2 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (5 mol %), and K_2CO_3 (3.0 equiv.). Then THF/H_2O (3/1 V/V) was added via syringe, and the mixture was placed into a preheated oil bath at 80 °C and stirred at for 3 hours. After cooling to r.t., DCM was added to the mixture, extracted and dried over $MgSO_4$. The combined organic layers were evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel using cyclohexane and ethyl acetate as eluent (8:2 to 2:8) to afford the corresponding starting material.

*2-Chloro-3-nitro-6-phenylimidazo[1,2-a]pyridine (**2c**)*. Yellow solid (246 mg, 90%); mp 160-165 °C; IR (film, cm^{-1}): 1517, 1499, 1476, 1452, 1440, 1415, 1344, 1322, 1213, 823, 766, 747, 698; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.60 (s, 1H), 7.93 (d, J = 9.2 Hz, 1H), 7.82 (d, J = 9.2 Hz, 1H), 7.61 (d, J = 7.2 Hz, 2H), 7.56 – 7.48 (m, 3H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 142.6, 140.3, 135.7, 132.0, 129.6 (2CH), 129.3, 127.4 (2CH), 125.3, 124.6, 123.0, 117.7; HRMS (ESI): for $C_{13}H_9ClN_3O_2$ $(M + H)^+$: m/z calcd. 274.0383, found 274.0377.

*2-Chloro-6-(4-methoxyphenyl)-3-nitroimidazo[1,2-a]pyridine (**2d**)*. Yellow solid (279 mg, 92%); mp. 170-175 °C; IR (film, cm^{-1}): 1485, 1472, 1424, 1406, 1342, 1319, 1283, 1248, 1209, 1179, 823, 812; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.54 (s, 1H), 7.89 (d, J = 9.2 Hz, 1H), 7.78 (d, J = 9.2 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.04 (d, J = 8.6 Hz, 2H), 3.88 (s, 3H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 160.7, 142.5, 140.2, 138.8, 131.8, 131.7, 128.6 (2CH), 127.9,

124.7, 117.6, 115.1 (2CH), 55.6 (OCH_3); HRMS (ESI): for $C_{14}H_{11}ClN_3O_3$ $(M + H)^+$: *m*/*z* calcd. 304.0489, found 304.048

2-Chloro-3-nitro-6-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine ***(2e)***. Yellow solid (324 mg, 95%); mp 172-176 °C; IR (film, cm^{-1}): 1497, 1474, 1409, 1344, 1325, 1214, 824, 814. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1H), 7.96-7.76 (m, 6H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 148.3, 137.3, 136.5, 132.2 (d, J = 270 Hz), 130.8 (q, J = 30 Hz), 125.5, 121.7, 131.5, 127.9 (2CH), 126.7 (q, J = 3.5 Hz, 2CH), 125.8 (CH), 118.1 (CH); $^{19}F\{1H\}$ NMR (188 MHz, $CDCl_3$) δ -62.8; HRMS (ESI): for $C_{14}H_8ClF_3N_3O_2$ $(M + H)^+$: *m*/*z* calcd. 342.0257, found 342.0257.

General procedure for the preparation of compounds 3a-s:

A 10 mL sealed tube under argon atmosphere was charged with *N*-tosylhydrazone (1.0 mmol, 1.0 equiv), 2-chloro-3-nitroimidazo[1,2-*a*]pyridine (1.0 mmol, 1.0 equiv.), $Pd_2dba_3 \cdot CHCl_3$ (2.5 mol %), and XPhos (5 mol %). Then dioxane (4.0 mL) was added via syringe, and the mixture was stirred at room temperature for 1 minute before the addition of Li*O*t*Bu (2.2 mmol, 2.2 equiv.). Then the tube was put into microwave and stirred at 110 °C for 30 minutes. After cooling to r.t., DCM was added to the mixture. The solvents were evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel using cyclohexane and ethyl acetate (7:3 to 3:7) as eluent to afford the desired product.

3-Nitro-2-(1-phenylvinyl)imidazo[1,2-a]pyridine ***(3a).*** Yellow solid (216 mg, 82% yield); mp 100-102 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1481, 1462, 1378, 1363, 1329, 1312, 1208, 1129, 744, 731, 694; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm). 9.45 (d, J = 7.0 Hz, 1H), 7.86 (d, J = 8.9 Hz, 1H), 7.68-7.63 (m, 1H), 7.36-7.30 (m, 6H), 6.02 (s, 1H), 5.76 (s, 1H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 150.5, 145.2, 141.9, 138.5, 137.4, 130.7, 128.6 (2CH), 128.3, 127.9, 126.4 (2CH), 120.0, 118.6, 116.7. HRMS (ESI): for $C_{15}H_{12}N_3O_2$ $(M + H)^+$: *m*/*z* calcd. 266.0930, found 266.0934.

*2-(1-(Naphthalen-2-yl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3b**).* Yellow solid (272 mg, 86% yield); mp 171-172 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1481, 1461, 1382, 1364, 1328, 1312, 1210, 1132, 819, 768, 744, 731; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.45 (d, J = 7.0 Hz, 1H), 7.89 (d, J = 8.9 Hz, 1H), 7.83-7.79 (m, 2H), 7.73-7.66 (m, 3H), 7.63-7.59 (m, 1H), 7.46-7.39 (m, 2H), 7.30-7.25 (m, 1H), 6.15 (s, 1H), 5.84 (s, 1H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 150.6, 145.2, 141.9, 135.9, 133.4, 133.3, 130.8, 128.4 (2CH), 127.9, 127.8, 126.3, 126.2, 125.4, 124.5, 120.4 (CH_2), 118.6, 116.8; HRMS (ESI): for $C_{19}H_{14}N_3O_2$ $(M + H)^+$: *m/z* calcd. 316.1086, found 316.1084.

*3-Nitro-2-(1-(phenanthren-3-yl)vinyl)imidazo[1,2-a]pyridine (**3c**).* Yellow solid (328 mg, 90% yield); mp 244-245 °C; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1480, 1463, 1375, 1329, 1312, 1209, 1122, 919, 844, 739, 712; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.47 (d, J = 7.0 Hz, 1H), 8.64 (s, 1H), 8.57-8.54 (m, 1H), 7.92 (d, J = 8.9 Hz, 1H), 7.88-7.84 (m, 2H), 7.72 (s, 2H), 7.69-7.56 (m, 4H), 7.31 (t, J = 7.0 Hz, 1H), 6.20 (s, 1H), 5.92 (s, 1H).$^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 150.6, 142.3, 136.9, 132.4, 132.0, 130.81, 130.5, 130.4, 128.9, 128.8, 128.0, 127.4, 126.8, 126.7, 126.6, 125.7, 125.4, 122.9, 121.0 (CH_2), 120.6, 118.7, 116.8. HRMS (ESI): for $C_{23}H_{16}N_3O_2$ $(M + H)^+$: *m/z* calcd. 366.1243, found 366.1248.

*2-(1-(4-Methoxyphenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine **(3d).*** Yellow solid (274 mg, 93% yield); mp 132-133 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 2837, 1510, 1462, 1377, 1364, 1328, 1313, 1253, 1245, 1206, 1179, 1130, 1030, 836, 819, 769, 746; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.43 (d, J = 6.9 Hz, 1H), 7.84 (d, J = 9.0 Hz, 1H), 7.66-7.60 (m, 1H), 7.27-7.25 (m, 3H), 6.82 (d, J = 8.6 Hz, 2H), 5.90 (s, 1H), 5.62 (s, 1H), 3.77 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 159.7, 150.8, 145.2, 141.2, 131.1, 130.7, 127.9, 127.6 (2CH), 118.5, 118.2 (CH_2), 116.7, 114.0 (2CH), 55.4 (OCH_3). HRMS (ESI): for $C_{16}H_{14}N_3O_3$ $(M + H)^+$: *m/z* calcd. 296.1035, found 296.1027.

3-Nitro-2-(1-(3,4,5-trimethoxyphenyl)vinyl)imidazo[1,2-a]pyridine ***(3e).*** Yellow solid (287 mg, 81% yield); mp 171-173 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1581, 1525, 1506, 1483, 1380, 1366, 1323, 1242, 1210, 1126; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.40 (d, *J* = 7.0 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 7.0 Hz, 1H), 6.55 (s, 2H), 5.92 (s, 1H), 5.68 (s, 1H), 3.81 (s, 3H), 3.77 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 153.3 (2C), 150.3, 145.1, 141.7, 138.6, 134.4, 130.8, 127.9, 120.0 (CH_2), 118.6, 116.8, 104.5 (2CH), 61.0 (OCH_3), 56.4 ($2OCH_3$). HRMS (ESI): for $C_{18}H_{18}N_3O_5$ $(M + H)^+$: *m/z* calcd. 356.1246, found 356.1240.

3-Nitro-2-(1-(2,3,4-trimethoxyphenyl)vinyl)imidazo[1,2-a]pyridine ***(3f).*** Yellow solid (321 mg, 90% yield); mp 100-102 ºC; R_f = 0.41 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1496, 1482, 1463, 1380, 1364, 1329, 1297, 1209,1095; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.35 (d, *J* = 6.9 Hz, 1H), 7.76 (d, *J* = 8.9 Hz, 1H), 7.58-7.53 (m, 1H), 7.18 (t, *J* = 6.9 Hz, 1H), 7.05 (d, *J* = 8.6 Hz, 1H), 6.65 (d, *J* = 8.7 Hz, 1H), 5.91 (s, 1H), 5.86 (s, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.55 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 153.7, 151.7, 151.3, 144.7, 142.2, 138.8, 130.5, 127.7, 126.3, 124.2, 122.9 (CH_2), 118.1, 116.3, 107.5, 60.8 (OCH_3), 60.7 (OCH_3), 55.9 (OCH_3). HRMS (ESI): for $C_{18}H_{18}N_3O_5$ $(M + H)^+$: *m/z* calcd. 356.1246, found 356.1247.

2-(1-(3,5-Dimethoxyphenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine ***(3g).*** Yellow solid (305 mg, 94% yield); mp 182-184 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1513, 1482, 1463, 1375, 1328, 1314, 1263, 1210, 1144, 1128, 1024, 769, 746; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.41 (d, *J* = 6.9 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.66-7.60 (m, 1H), 7.26 (t, *J* = 7.0 Hz, 1H), 6.48 (d, *J* = 2.1 Hz, 2H), 6.40-6.38 (m, 1H), 6.00 (s, 1H), 5.73 (s, 1H), 3.74 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 160.8 (2C), 150.2, 145.1, 141.7, 140.5, 130.7, 127.8, 120.1 (CH_2), 118.5, 116.7, 105.1 (2CH), 99.9, 55.4 ($2OCH_3$). HRMS (ESI): for $C_{17}H_{16}N_3O_4$ $(M + H)^+$: *m/z* calcd. 326.1141, found 326.1148.

*2-(1-(3,4-Dimethoxyphenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3h**).* Yellow solid (312 mg, 96% yield); mp 177-179 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1513, 1482, 1375, 1329, 1314, 1263, 1245, 1210, 1144, 1128, 1024, 769, 747; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.41 (d, J = 6.9 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.63 (t, J = 7.9 Hz, 1H), 7.26 (t, J = 6.9 Hz, 1H), 6.98 (s, 1H), 6.80-6.73 (m, 2H), 5.91 (s, 1H), 5.64 (s, 1H), 3.84 (s, 3H), 3.83 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 150.5, 149.4, 149.0, 145.0, 141.3, 131.4, 130.7, 127.8, 119.2, 118.5, 118.4 (CH_2), 116.6, 1101.0, 109.8, 56.1 (OCH_3), 55.9 (OCH_3). HRMS (ESI): for $C_{17}H_{16}N_3O_4$ $(M + H)^+$: *m/z* calcd. 326.1141, found 326.1142.

*3-Nitro-2-(1-(p-tolyl)vinyl)imidazo[1,2-a]pyridine (**3i**).* yellow solid (252 mg, 90% yield); mp 129-131 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1480, 1463, 1376, 1362, 1328, 1312, 1209, 1129, 819, 768, 745,725; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.43 (d, J = 7.0 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.64 (t, J = 8.4 Hz, 1H), 7.28-7.22 (m, 3H), 7.11 (d, J = 7.9 Hz, 2H), 5.97 (s, 1H), 5.69 (s, 1H), 2.32 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 150.7, 145.1, 141.7, 138.0 (2C), 135.6, 130.7, 129.2 (2CH), 127.8, 126.2 (2CH), 119.1, 118.5, 116.6, 21.3. HRMS (ESI): for $C_{16}H_{14}N_3O_2$ $(M + H)^+$: *m/z* calcd. 280.1086, found 280.1082.

*2-(1-(4-Fluorophenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3j**).* Yellow solid (237 mg, 84% yield); mp 152-153 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1508, 1482, 1378, 1329, 1314, 1212, 1160, 1130, 842, 820, 771, 746; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.43 (d, J = 6.8 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.68-7.62 (m, 1H), 7.34-7.28 (m, 3H), 6.98 (t, J = 8.2 Hz, 2H), 5.95 (s, 1H), 5.73 (s, 1H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 164.4, 162.7 (d, J = 247.5 Hz), 150.2, 145.1, 140.8, 134.6, 130.8, 128.1 (d, J = 8.1, 2CH), 127.8, 119.9, 118.5, 116.8, 115.4 (d, J = 21.7 Hz, 2CH); $^{19}F\{1H\}$ NMR (188 MHz, CDCl3) δ -113.89; HRMS (ESI): for $C_{15}H_{11}N_3O_2F$ $(M + H)^+$: *m/z* calcd. 284.0835, found 284.0834.

*3-Nitro-2-(1-(3,4,5-trifluorophenyl)vinyl)imidazo[1,2-a]pyridine (**3k**).* yellow solid (299 mg, 94% yield); mp 153-155 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1528,

1483, 1441, 1384, 1370, 1331, 1313, 1208, 1129, 1041, 784, 768, 747; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.44 (d, J = 7.0 Hz, 1H), 7.86 (d, J = 8.9 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.32 (t, J = 7.0 Hz, 1H), 6.98 – 6.93 (m, 2H), 5.97 (s, 1H), 5.82 (s, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 151.3 (ddd, J = 249.7, 10.1, 4.0 Hz, 2C), 148.7, 145.2, 139.6 (dt, J = 252.9, 15.5, Hz), 139.4, 134.8 (q, J = 12 Hz), 131.1, 127.9, 122.0, 118.6, 117.1, 110.7 (d, J = 21.9 Hz, 2CH), 110.71 (d, J = 8.2 Hz); ^{19}F{1H} NMR (188 MHz, $CDCl_3$) δ -134.26 (d, J = 20.4 Hz), -160.73 (t, J = 20.5 Hz); HRMS (ESI): for $C_{15}H_9N_3O_2F_3$ $(M + H)^+$: *m/z* calcd. 320.0647, found 320.0645.

*2-(1-(4-Chlorophenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3l**).* Yellow solid (219 mg, 73% yield); mp 170-172 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1523, 1479, 1377, 1368, 1328, 1313, 1210, 1128, 1104, 766, 746. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): ^{1}H NMR (300 MHz, $CDCl_3$-*d*) δ 9.38 (d, J = 6.9 Hz, 1H), 7.80 (d, J = 8.9 Hz, 1H), 7.64-7.58 (m, 1H), 7.18-7.26 (m, 5H), 5.94 (s, 1H), 5.73 (s, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.9, 145.1, 140.8 (2C), 137.0, 134.0, 130.9, 128.7 (2CH), 127.8, 127.7 (2CH), 120.5, 118.5, 116.8. HRMS (ESI): for $C_{15}H_{11}ClN_3O_2$ $(M + H)^+$: *m/z* calcd. 300.0540, found 300.0537.

*4-(1-(3-Nitroimidazo[1,2-a]pyridin-2-yl)vinyl)benzonitrile (**3m**).* Yellow solid (255 mg, 87%, yield); mp 214-216 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1527, 1482, 1380, 1330, 1314, 1212, 1130, 848, 820, 769, 747; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.44 (d, J = 6.9 Hz, 1H), 7.87 (d, J = 8.9 Hz, 1H), 7.72-7.67 (m, 1H), 7.60 (d, J = 7.4 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 7.32 (t, J = 7.0 Hz, 1H), 6.09 (s, 1H), 5.93 (s, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.0, 145.3, 143.0, 140.6, 132.5 (2CH), 131.1, 127.9, 127.1 (2CH), 123.1, 118.8, 118.8, 118.6, 117.1, 111.8; HRMS (ESI): for $C_{16}H_{11}N_4O_2$ $(M + H)^+$: *m/z* calcd. 291.0882, found 291.0887.

*2-(1-([1,1'-Biphenyl]-4-yl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3n**).* Yellow solid (290 mg, 85% yield); mp 209-211 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1483,

1379, 1365, 1330, 1313, 1213, 1129, 764, 741, 698; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.46 (d, J = 6.8 Hz, 1H), 7.87 (d, J = 8.9 Hz, 1H), 7.68-7.63 (m, 1H), 7.59-7.54 (m, 4H), 7.44-7.39 (m, 4H), 7.34 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 6.9 Hz, 1H), 6.08 (s, 1H), 5.78 (s, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 150.5, 145.2, 141.4 (2C), 141.1, 140.8, 137.4, 130.8, 128.9 (2CH), 127.9, 127.5, 127.3 (2CH), 127.2 (2CH), 126.8 (2CH), 119.9, 118.6, 116.8; HRMS (ESI): for $C_{21}H_{16}N_3O_2$ $(M + H)^+$: *m/z* calcd. 342.1243, found 342.1248.

*3-Nitro-2-(1-(pyridin-3-yl)vinyl)imidazo[1,2-a]pyridine (**3o**).* Yellow solid (213 mg, 80% yield); mp 163-165 ºC; R_f = 0.3 (cyclohexane/acetone 5/5); IR (film, cm^{-1}): 1633, 1524, 1483, 1380, 1368, 1330, 1313, 1211, 1131,819, 767, 747, 714; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.38 (d, J = 6.6 Hz, 1H), 8.55 (d, J = 2.0 Hz, 1H), 8.47 (d, J = 4.5 Hz, 1H), 7.81 (d, J = 8.6 Hz, 1H), 7.66-7.61 (m, 2H), 7.26 (t, J = 7.0 Hz, 1H), 7.22-7.18 (m, 1H), 6.01 (s, 1H), 5.84 (s, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.2, 147.6, 145.1, 139.0 (2C), 134.2 (2C), 133.6, 131.0, 127.8, 123.2, 121.9, 118.5, 116.9. HRMS (ESI): for $C_{14}H_{11}N_4O_2$ $(M + H)^+$: *m/z* calcd. 267.0882, found 267.0888.

*9-Methyl-3-(1-(3-nitroimidazo[1,2-a]pyridin-2-yl)vinyl)-9H-carbazole (**3p**).* Yellow solid (351 mg, 95% yield); mp 127-129 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1481, 1463, 1379, 1364, 1329, 1314, 1251, 1212, 1128, 768, 747, 730; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.38 (d, J = 6.9 Hz, 1H), 8.04 (s, 1H), 7.98 (d, J = 7.7 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.61 – 7.58 (m, 2H), 7.45 – 7.40 (m, 1H), 7.30 – 7.28 (m, 2H), 7.17 (q, J = 7.6, 7.1 Hz, 2H), 6.07 (s, 1H), 5.74 (s, 1H), 3.77 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 151.3, 145.1, 142.4, 141.4, 140.9, 130.6, 129.6 (2C), 127.8, 125.8, 124.6, 122.8 (2C), 120.4, 119.0, 118.4, 118.3, 118.1, 116.6, 108.6, 108.4, 29.12 (NCH_3). HRMS (ESI): for $C_{22}H_{17}N_4O_2$ $(M + H)^+$: *m/z* calcd. 369.1352, found 369.1348.

*2-(3,4-Dihydronaphthalen-1-yl)-3-nitroimidazo[1,2-a]pyridine (**3q**).* Yellow solid (253 mg, 87% yield); mp 94-96 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1524, 1481,

1439, 1384, 1364, 1332, 1312, 1206, 1134, 764, 735; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.45 (d, J = 6.9 Hz, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.63-7.58 (m, 1H), 7.25 (d, J = 6.8 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.13 (t, J = 7.3 Hz, 1H), 7.02 (t, J = 7.4 Hz, 1H), 6.76 (d, J = 7.6 Hz, 1H), 6.47 (t, J = 4.5 Hz, 1H), 2.94 (t, J = 8.0 Hz, 2H), 2.52 (td, J_1 = 7.9, J_2 =4.9 Hz, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.4, 145.3, 135.5 (2C), 132.9, 132.2 (2C), 130.6, 127.9, 127.8, 127.5, 126.4, 123.4, 118.3, 116.5, 27.7, 23.5; HRMS (ESI): for $C_{17}H_{14}N_3O_2$ $(M + H)^+$: *m/z* calcd. 292.1086, found 292.1083.

3-Nitro-2-(2H-thiochromen-4-yl)imidazo[1,2-a]pyridine ***(3r).*** Yellow solid (257 mg, 83% yield); mp 203-205 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1628, 1525, 1484, 1438, 1382, 1367, 1335, 1314, 1270, 1212, 1127, 765, 733; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.46 (d, J = 7.0 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.68-7.63 (m, 1H), 7.37 (d, J = 7.7 Hz, 1H), 7.29 (t, J = 7.3 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 6.42 (t, J = 5.6 Hz, 1H), 3.56 (s, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.2, 145.2, 133.7 (2C), 132.9, 132.4, 130.8, 128.3, 127.9 (2CH), 126.5, 125.8, 125.5, 118.5, 116.8, 25.2 (SCH_2). HRMS (ESI): for $C_{16}H_{12}N_3O_2S$ $(M + H)^+$: *m/z* calcd. 310.0650, found 310.0646.

2-(2H-Chromen-4-yl)-3-nitroimidazo[1,2-a]pyridine ***(3s).*** Yellow solid (249 mg, 85% yield); mp 187-189 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1527, 1483, 1441, 1387, 1367, 1334, 1314, 1220, 1204, 1133, 1123, 822, 763, 747; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.49 (d, J = 7.0 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.70-7.64 (m, 1H), 7.31 (t, J = 7.0 Hz, 1H), 7.17-7.12 (m, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.78 (d, J = 4.2 Hz, 2H), 6.19 (t, J = 3.8 Hz, 1H), 5.00 (d, J = 3.8 Hz, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 154.0, 146.8, 145.4, 133.3, 130.9, 129.8, 129.3 (2C), 128.0, 125.5, 124.4, 121.5, 118.6, 116.9, 116.6, 65.3 (OCH_2). HRMS (ESI): for $C_{16}H_{12}N_3O_3$ $(M + H)^+$: *m/z* calcd. 294.0879, found 294.0874.

2-(2,2-Bis(4-methoxyphenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3t**). Yellow solid (273 mg, 68% yield); mp 153-155 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1606, 1512, 1483, 1382, 1366, 1330, 1314, 1248, 1213, 1177, 1031, 766, 746; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.48 (d, J = 7.0 Hz, 1H), 7.86 (d, J = 9.3 Hz, 1H), 7.67 (ddd, J = 8.9, 7.1, 1.3 Hz, 1H), 7.35-7.25 (m, 3H), 7.18 (s, 1H), 6.98 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.67 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H), 3.74 (s, 3H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 159.3, 158.9, 150.0, 145.8, 145.4, 134.1, 132.8, 131.5, 131.3, 131.0, 130.9, 130.4, 129.9, 129.3, 128.0, 118.5, 116.4, 116.2, 113.9, 113.7, 113.5, 55.29, 55.13. HRMS (ESI): for $C_{23}H_{20}N_3O_2$ $(M + H)^+$: *m*/*z* calcd. 402.1454, found 402.1457.

2-(1-(4-Methoxyphenyl)vinyl)-3-nitro-6-(4-(trifluoromethyl)phenyl)imidazo[1,2-a] pyridine ***(3u).*** Yellow solid (386 mg, 88% yield); mp 173-175 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1512, 1482, 1463, 1322, 1258, 1247, 1211, 1166, 1128, 1112, 1073, 819; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1H), 8.97-7.87 (m, 2H), 7.82-7.75 (m, 4H), 7.29 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 5.94 (s, 1H), 5.67 (s, 1H), 3.79 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 159.8, 151.4, 144.4, 141.2 (2C), 139.8, 131.2 (q, J = 32 Hz), 131.0, 130.6, 129.9, 127.8 (2CH), 127.7 (2CH), 126.6, 126.5, 125.8, 124.0 (d, J = 270 Hz), 118.7, 118.4, 114.0 (2CH), 55.4; ^{19}F{1H} NMR (188 MHz, $CDCl_3$) δ -62.72; HRMS (ESI): for $C_{23}H_{17}F_3N_3O_3$ $(M + H)^+$: *m*/*z* calcd. 440.1222, found 440.1219.

6-(4-Methoxyphenyl)-2-(1-(4-methoxyphenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine ***(3v).*** Yellow solid (363 mg, 90% yield): R_f = 0.25 (cyclohexane/ethyl acetate 7/3); mp 159-160 ºC; IR (film, cm^{-1}): 1608, 1511, 1484, 1464, 1381, 1319, 1257, 1244, 1207, 1180, 1034,838, 818; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.59 (s, 1H), 7.87 (s, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 5.92 (s, 1H), 5.65 (s, 1H), 3.88 (s, 3H), 3.79 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 160.5, 159.7, 151.0, 144.2, 141.4 (2C), 131.2 (2C), 131.0, 128.6 (2CH), 127.7 (2CH), 124.6, 118.2, 118.1, 115.0 (2CH),

114.0 (2CH), 55.6 (OCH_3), 55.4 (OCH_3). HRMS (ESI): for $C_{23}H_{20}N_3O_4$ $(M + H)^+$: *m/z* calcd. 402.1454, found 402.1447.

*2-(1-(4-Methoxyphenyl)vinyl)-3-nitro-6-phenylimidazo[1,2-a]pyridine (**3w**).* Yellow solid (342 mg, 92% yield); mp 147-149 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1607, 1512, 1475, 1381, 1352, 1322, 1247, 1209, 1181, 1032, 834; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.63 (s, 1H), 7.90 (s, 2H), 7.65-7.62 (m, 3H), 7.58-7.39 (m, 4H), 7.30 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 5.93 (s, 1H), 5.66 (s, 1H), 3.79 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 159.7, 151.1, 144.3, 141.3 (2C), 136.1, 131.4 (2C), 131.1, 129.5 (2CH), 129.0, 127.6 (2CH), 127.4 (2CH), 125.2, 118.2, 118.1, 114.0 (2CH), 55.3 (OCH_3). HRMS (ESI): for $C_{22}H_{18}N_3O_3$ $(M + H)^+$: *m/z* calcd. 372.1348, found 372.1354.

*2,6-Bis(1-(4-methoxyphenyl)vinyl)-3-nitroimidazo[1,2-a]pyridine (**3x**).* Yellow solid (384 mg, 89% yield): mp 150-152 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1606, 1510, 1483, 1460, 1331,1244, 1207, 1178, 1028, 834, 817, 733; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.43 (s, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.59 (d, J = 9.2 Hz, 1H), 7.29 (d, J = 2.6 Hz, 2H), 7.26 (d, J = 2.6 Hz, 2H), 6.90 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 5.91 (s, 1H), 5.64 (s, 1H), 5.59 (s, 1H), 5.50 (s, 1H), 3.83 (s, 3H), 3.78 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 160.2, 159.7, 151.0, 145.0 (2C), 144.6, 141.3 (2C), 132.0, 131.9, 131.1, 129.3 (2CH), 127.6 (2CH), 126.4, 118.2, 117.5, 115.8, 114.2 (2CH), 114.0 (2CH), 55.5 (OCH_3), 55.4 (OCH_3). HRMS (ESI): for $C_{25}H_{22}N_3O_4$ $(M + H)^+$: *m/z* calcd. 428.1610, found 428.1599.

*2,6-Bis(3,4-dihydronaphthalen-1-yl)-3-nitroimidazo[1,2-a]pyridine (**3y**).*Yellow solid (302 mg, 72% yield); mp 210-211 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1525, 1485, 1464, 1418, 1386, 1356, 1320, 1211, 737, 701; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.50 (s, 1H), 7.81 (d, J = 9.1 Hz, 1H), 77.63 (dd, J = 9.0, 1.7 Hz, 1H), 7.25-7.13 (m, 5H), 7.07 (t, J = 7.3 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 6.51 (t, J = 4.6 Hz, 1H), 6.28 (t, J = 4.6 Hz, 1H), 3.01-2.90 (m, 4H), 2.59-2.48 (m, 4H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$)

δ (ppm):157.2, 136.8, 135.8, 135.7, 135.6, 135.5, 133.9, 133.0, 132.8, 132.4, 132.3, 130.9, 130.8, 128.2, 128.1, 127.9, 127.6, 126.8, 126.6, 126.5, 125.0, 123.6, 117.4, 28.0, 27.8, 23.7, 23.6; HRMS (ESI): for $C_{27}H_{22}N_3O_2$ $(M + H)^+$: *m/z* calcd. 420.1712, found 420.1707.

*2,6-Di(2H-chromen-4-yl)-3-nitroimidazo[1,2-a]pyridine (**3z**)* Yellow solid (326 mg, 77% yield); mp 223-224 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1484, 1420, 1389, 1345, 1321, 1225, 1205, 1065, 733; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.51 (s, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.65-7.62 (m, 1H), 7.25-7.20 (m, 1H), 7.18-7.13 (m, 1H), 6.97-6.87 (m, 4H), 6.82-6.77 (m, 2H), 6.22 (t, *J* = 3.8 Hz, 1H), 6.00 (t, *J* = 3.9 Hz, 1H), 5.01 (d, *J* = 3.8 Hz, 2H), 4.92 (d, *J* = 3.9 Hz, 2H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 157.9, 154.8, 147.1, 132.8, 132.2, 131.3, 131.3, 130.4, 129.9, 129.3, 128.6 (2C), 126.6, 125.6, 125.2, 124.4, 122.9, 122.5 (2C), 121.8, 121.5, 117.9, 116.9, 116.6, 65.3, 65.1; HRMS (ESI): for $C_{25}H_{18}N_3O_4$ $(M + H)^+$: *m/z* calcd. 424.1297, found 424.1288.

General procedure for the preparation of compounds 4.[26]

Iron powder (112 mg, 2 mmol, 10 equiv.) and concd hydrochloric acid (*ca*. 1 μL) were added to a solution of nitro-compound (0.2 mmol) in EtOH (0.5 mL) and water (120 µL), and the mixture was heated to reflux in an oil bath for 90 min. DCM (20 mL) was added to the mixture, and it was dried with $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by chromatography to give the amino product.

*2-(1-Phenylvinyl)imidazo[1,2-a]pyridin-3-amine (**4a**).* Yellow solid (43 mg, 92% yield); mp 76-77 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1657, 1637, 1597, 1573, 1523, 1493, 1435, 1349, 1299, 1279, 898, 757, 732; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.83 (d, *J* = 6.4 Hz, 1H), 7.51 (d, *J* = 9.1 Hz, 1H), 7.45-7.34 (m, 5H), 7.10 – 7.05 (m, 1H), 6.75 (t, *J* = 6.7 Hz, 1H), 5.93 (s, 1H), 5.50 (s, 1H), 2.89 (s, 2H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm):

141.9, 140.3, 140.3, 128.8 (2CH), 128.2, 128.0 (2CH), 125.1, 123.8, 122.2, 122.0, 117.1, 116.5, 112.0; HRMS (ESI): for $C_{15}H_{14}N_3$ $(M + H)^+$: *m/z* calcd. 236.1188, found 236.1189.

*2-(1-(Phenanthren-3-yl)vinyl)imidazo[1,2-a]pyridin-3-amine (**4b**).* Yellow solid (61 mg, 91% yield); mp 177-179 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1657, 1636, 1601, 1506, 1453, 1435, 1378, 1350, 1268, 1241, 844, 750, 732; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.76 (s, 1H), 8.64 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 2H), 7.82 (d, *J* = 6.9 Hz, 1H), 7.68 (s, 2H), 7.65-7.53 (m, 4H), 7.12-7.06 (m, 1H), 6.75 (t, *J* = 6.7 Hz, 1H), 6.09 (s, 1H), 5.68 (s, 1H), 2.87 (s, 2H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 139.5, 138.1, 137.0, 132.3, 132.0, 130.4, 130.1, 129.1, 128.7, 127.7, 127.2, 127.1, 127.0, 126.9, 126.8, 126.4, 126.2, 123.5, 122.8, 122.0, 118.2, 114.6, 113.6. HRMS (ESI): for $C_{23}H_{18}N_3$ $(M + H)^+$: *m/z* calcd. 336.1501, found 336.1504.

*2-(1-(3,4,5-Trimethoxyphenyl)vinyl)imidazo[1,2-a]pyridin-3-amine (**4c**).* Yellow solid (61 mg, 94% yield); mp 123-125 ºC; R_f = 0.25 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 2937, 1579, 1504, 1465, 1411, 1323, 1235, 1125, 1005, 733; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.82 (d, *J* = 6.7 Hz, 1H), 7.49 (d, *J* = 9.1 Hz, 1H), 7.08-7.03 (m, 1H), 6.74 (t, *J* = 6.8 Hz, 1H), 6.64 (s, 2H), 5.87 (s, 1H), 5.45 (s, 1H), 3.86 (s, 3H), 3.81 (s, 6H), 3.0 (s, 2H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 153.5, 142.2 (2C), 140.5, 138.1, 136.2, 130.1, 125.2, 123.3, 121.8, 117.4, 115.6, 111.8, 105.23 (2CH), 61.0 (OCH_3), 56.3 ($2OCH_3$). HRMS (ESI): for $C_{18}H_{20}N_3O_3$ $(M + H)^+$: *m/z* calcd. 326.1505, found. 326.1503.

*2-(1-(3,5-Dimethoxyphenyl)vinyl)imidazo[1,2-a]pyridin-3-amine (**4d**).* Yellow solid (56 mg, 95% yield); mp 145-147 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 2837,1605, 1587, 1454, 1422, 1316, 1299, 1204, 1154, 1064, 1046, 836, 753, 732; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.82 (d, *J* = 6.8 Hz, 1H), 7.49 (d, *J* = 9.1 Hz, 1H), 7.09-7.04 (m, 1H), 6.74 (t, *J* = 6.7 Hz, 1H), 6.58 (d, *J* = 2.2 Hz, 2H), 6.47-6.46 (m, 1H), 5.94 (s, 1H), 5.48 (s, 1H), 3.77 (s, 6H), 2.99 (s, 2H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 161.2 (2C), 142.1, 141.4, 139.8,

128.0, 125.6, 124.4, 122.4, 116.6, 116.5, 112.3, 106.1 (2CH), 100.4, 55.6 ($2OCH_3$). HRMS (ESI): for $C_{17}H_{18}N_3O_2$ $(M + H)^+$: *m/z* calcd. 296.1399, found 296.1398.

*2-(1-(3,4,5-Trifluorophenyl)vinyl)imidazo[1,2-a]pyridin-3-amine (**4e**).* Yellow solid (56 mg, 97% yield); mp 93-95 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1619, 1526, 1435, 1332, 1235, 1041, 862, 781, 740, 697; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.88 (d, *J* = 6.9 Hz, 1H), 7.46 (d, *J* = 9.1 Hz, 1H), 7.10-7.03 (m, 3H), 6.78 (t, *J* = 6.7 Hz, 1H), 5.75 (s, 1H), 5.60 (s, 1H), 3.23 (s, 2H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 151.23 (dd, *J* = 252.0, 11.7 Hz), 139.4 (2C), 138.7, 136.84 (d, *J* = 176.7 Hz), 126.4, 126.0, 125.3, 122.8, 118.2, 116.1, 112.9, 112.0 (d, *J* = 21.6 Hz, 2C), 112.0 (d, *J* = 8.2 Hz); $^{19}F\{1H\}$ NMR (188 MHz, $CDCl_3$) *δ* -133.92 (d, *J* = 20.6 Hz), -160.53 (t, *J* = 20.6 Hz); HRMS (ESI): for $C_{15}H_{11}F_3N_3$ $(M + H)^+$: *m/z* calcd. 290.0905, found 290.0903.

*2-(2H-Thiochromen-4-yl)imidazo[1,2-a]pyridin-3-amine (**4f**).* Yellow solid (45 mg, 80% yield); mp 153-155 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1640, 1586, 1515, 1467, 1433, 1358, 1331, 1270, 1145, 769, 731; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.03 (d, *J* = 6.9 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.39 (d, *J* = 7.1 Hz, 1H), 7.21-7.10 (m, 4H), 6.87 (t, *J* = 6.8 Hz, 1H), 6.52 (t, *J* = 5.8 Hz, 1H), 3.49 (d, *J* = 5.9 Hz, 2H), 2.24 (s, 2H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 140.5, 133.9, 133.5, 132.5, 130.4, 128.3, 128.0, 127.2, 125.9, 124.4, 124.1, 123.5, 122.0, 117.2, 112.1, 25.5 (SCH_2). HRMS (ESI): for $C_{16}H_{14}N_3S$ $(M + H)^+$: *m/z* calcd. 280.0908, found 280.0910.

*2-(2H-Chromen-4-yl)imidazo[1,2-a]pyridin-3-amine (**4g**).* Yellow solid (43 mg, 82% yield); mp 157-159 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1639, 1604, 1579, 1523, 1486, 1448, 1376, 1331, 1225, 1066, 756, 733; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.29 (s, 1H), 8.04 (d, *J* = 5.7 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.21-7.09 (m, 3H), 6.91-6.88 (m, 2H), 6.15 (s, 1H), 5.77 (s, 2H), 4.86 (s, 2H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 154.7 (C), 139.0 (C), 123.0 (CH), 126.9 (C), 126.4 (CH), 125.7 (C), 125.2 (CH), 124.7 (CH), 123.2

(C), 122.9 (CH), 121.8 (CH), 121.6 (C), 116.8 (CH), 115.3 (CH), 113.7 (CH), 65.3 (OCH_2). HRMS (ESI): for $C_{16}H_{14}N_3O$ $(M + H)^+$: *m/z* calcd. 264.1137, found 264.1135.

General procedure for the preparation of compounds 5.

A 10 mL sealed tube under argon atmosphere was charged with compounds **3** (0.5 mmol, 1.0 equiv.) and PPh_3 (4 equiv.), and $MoO_2Cl_2(dmf)_2$ (10 mol%). Then dioxane (3.0 mL) was added via syringe. Then the tube was sealed and stirred at 135 °C under microwave irradiation for 4 hours. After cooling to r.t., DMAP (20 mol%), NEt_3 (3.0 equiv.) and $(Boc)_2O$ (0.65 mmol) was added and then the reaction mixture was stirred at r.t. for 2 hours. After completion (TLC), DCM was added to the reaction mixture and the solvents were evaporated under reduced pressure. Then the crude residue was purified by column chromatography on silica gel using cyclohexane and ethyl acetate as eluent to afford the desired product.

*Tert-butyl 3-phenyl-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5a**).* Yellow solid (136 mg, yield 82%); mp 146-147 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1727, 1519, 1354, 1288, 1270, 1204, 1155, 1109, 1064,741; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.25 (d, *J* = 7.5 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 9.3 Hz, 1H), 7.57 (s, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.19-7.14 (m, 1H), 6.78 (t, *J* = 6.9 Hz, 1H), 1.72 (s, 9H). $^{13}C\{1H\}$ NMR (95 MHz, $CDCl_3$) δ (ppm): 148.7, 147.6, 135.8, 132.7 (2C), 128.9 (2CH), 127.2, 126.4 (3CH), 123.7, 118.7, 117.9, 117.7, 110.7, 85.2, 28.3 ($3CH_3$). HRMS (ESI): for $C_{20}H_{20}N_3O_2$ $(M + H)^+$: *m/z* calcd. 334.1556, found 334.1552.

*Tert-butyl 3-(naphthalen-2-yl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5b**).* Yellow solid (178 mg, yield 93%); mp 172-174 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1727, 1520, 1371, 1353, 1338, 1284, 1203, 1154, 1108, 758,742; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (d, *J* = 5.2 Hz, 1H), 8.69 (s, 1H), 8.09-8.05 (m, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 9.3 Hz, 1H), 7.65 (s, 1H), 7.51-7.41 (m, 2H), 7.20-7.14 (m, 1H), 6.76 (t, *J* = 6.6 Hz, 1H), 1.73 (s, 9H).

^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 148.6, 147.6, 138.3, 134.0, 132.8, 130.1, 128.4 (2CH), 127.7, 126.2, 125.7, 125.2 (2CH), 124.2, 123.6, 119.0, 117.9, 117.6, 110.6, 85.2, 28.3 ($3CH_3$); HRMS (ESI): for $C_{24}H_{22}N_3O_2$ $(M + H)^+$: *m/z* calcd. 384.1712, found 384.1721.

*Tert-butyl 3-(phenanthren-3-yl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5c**)*. IR (film, cm^{-1}): 1727, 1519, 1353, 1286, 1203, 1154, 1109, 737. Yellow solid (195 mg, 90% yield); mp 185-187 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.46 (s, 1H), 9.24 (d, *J* = 3.4 Hz, 1H), 8.93 (d, *J* = 8.1 Hz, 1H), 8.28 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.78-7.70 (m, 5H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.21-7.16 (m, 1H), 6.77 (t, *J* = 6.8 Hz, 1H), 1.75 (s, 9H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 148.7, 147.6, 138.5, 132.4 (2C), 131.3 (2C), 131.0, 130.9, 130.5, 129.0, 128.5, 126.8, 126.7 (2CH), 126.7, 126.6, 124.9, 123.6, 123.4, 120.3, 118.9, 118.0, 110.6, 85.2, 28.3 ($3CH_3$); HRMS (ESI): for $C_{28}H_{24}N_3O_2$ $(M + H)^+$: *m/z* calcd. 434.1869, found 434.1870.

*Tert-butyl 3-(4-methoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5d**)*. Yellow solid (115 mg, 63% yield); mp 166-168 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1722, 1520, 1508, 1353, 1338, 1256, 1242, 1180, 1154, 1105, 1064,759, 742; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (s, 1H), 8.02 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 9.1 Hz, 1H), 7.46 (s, 1H), 7.17-7.12 (m, 1H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.76 (t, *J* = 6.6 Hz, 1H), 3.85 (s, 3H), 1.70 (s, 9H); ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ (ppm): 159.0, 148.8, 147.5, 138.3, 127.6 (2CH), 126.2, 125.4 (2C), 123.6, 117.8, 117.7, 117.4, 114.4 (2CH), 110.6, 82.2, 55.5 (OCH_3), 28.3 ($3CH_3$); HRMS (ESI): for $C_{21}H_{22}N_3O_3$ $(M + H)^+$: *m/z* calcd. 364.1661, found 364.1665.

*Tert-butyl 3-(3,4,5-trimethoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5e**)*. Yellow solid (165 mg, 78% yield); mp 118-120 ºC; R_f = 0.35 (cyclohexane/ ethyl acetate 5/5); IR (film, cm^{-1}): 1728, 1584, 1505, 1356, 1327, 1244, 1152, 1126, 1006, 732. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.23 (d, *J* = 3.6 Hz, 1H), 7.65 (d, *J* = 9.3 Hz, 2H), 7.46

(s, 1H), 7.32 (s, 2H), 7.15 (dd, *J* = 9.2, 6.8 Hz, 1H), 6.76 (t, *J* = 6.9 Hz, 1H), 4.00 (s, 6H), 3.89 (s, 3H), 1.71 (s, 9H); ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ (ppm): 153.7, 148.7, 147.5 (2C), 138.4, 137.8, 128.5 (2C), 128.2 (2C), 126.2, 123.5, 118.3, 118.0, 110.6, 104.1 (2CH), 85.3, 61.1 (OCH3), 56.5 (2OCH_3), 28.3 (3CH_3); HRMS (ESI): for $C_{23}H_{26}N_3O_5$ $(M + H)^+$: *m/z* calcd. 424.1872, found 424.1860.

*Tert-butyl 3-(2,3,4-trimethoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5f**)*. Yellow oil (160 mg, 76% yield); mp 130-132 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1723, 1465, 1353, 1200, 1154, 1106, 1089, 1026, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.26 (d, *J* = 5.9 Hz, 1H), 8.37 (d, *J* = 8.7 Hz, 1H), 7.91 (s, 1H), 7.67 (d, *J* = 9.3 Hz, 1H), 7.16-7.11 (m, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.76 (t, *J* = 6.8 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 3.90 (s, 3H), 1.70 (s, 9H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 152.8, 151.2, 148.9, 147.2, 142.8, 139.2, 126.2, 124.6, 123.4, 121.5, 119.6 (2C), 117.8, 113.4, 110.6, 108.1, 84.7, 61.0 (OCH_3), 60.1 (OCH_3), 56.2 (OCH_3), 28.2 (3CH_3). HRMS (ESI): for $C_{23}H_{26}N_3O_5$ $(M + H)^+$: *m/z* calcd. 424.1872, found 424.1869.

*Tert-butyl 3-(3,5-dimethoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5g**)*. Yellow solid (125 mg, 64% yield); mp178-180 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1725, 1610, 1518, 1355, 1286, 1248, 1203, 1152, 1108, 1065, 1048, 851, 760, 742; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.15 (d, *J* = 5.6 Hz, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.45 (s, 1H), 7.20 (d, *J* = 1.7 Hz, 2H), 7.10-7.05 (m, 1H), 6.68 (t, *J* = 6.9 Hz, 1H), 6.36 (s, 1H), 3.82 (s, 6H), 1.63 (s, 9H); ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ (ppm): 161.3 (2C), 148.7, 147.5, 138.3, 134.6 (2C), 126.2, 123.5, 119.1, 117.9, 117.8, 110.6, 104.7 (2CH), 99.6, 85.2, 55.6 (2OCH_3), 28.3 (3CH_3). HRMS (ESI): for $C_{22}H_{24}N_3O_4$ $(M + H)^+$: *m/z* calcd. 394.1767, found 394.1768.

*Tert-butyl 3-(3,4-dimethoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5h**)*. Yellow solid (138 mg, 70% yield); mp 160-164 ºC; R_f = 0.3

(cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1724, 1517, 1353, 1248, 1155, 1108, 1027, 762, 744; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (s, 1H), 7.70 (t, *J* = 9.5 Hz, 2H), 7.55 (d, *J* = 1.3 Hz, 1H), 7.45 (s, 1H), 7.18-7.13 (m, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.77 (t, *J* = 6.7 Hz, 1H), 4.02 (s, 3H), 3.92 (s, 3H), 1.71 (s, 9H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 149.4, 148.7, 148.6, 147.4, 138.2, 131.4, 126.2, 125.7 (2C), 123.6, 119.4, 117.9, 117.7, 111.8, 110.7, 109.7, 85.1, 56.3 (OCH_3), 56.1 (OCH_3), 28.3 ($3CH_3$). HRMS (ESI): for $C_{22}H_{24}N_3O_4$ $(M + H)^+$: *m/z* calcd. 394.1767, found 394.1766.

Tert-butyl 3-(p-tolyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate ***(5i)***. Yellow solid (108 mg, 62% yield); mp 175-177 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1724, 1520, 1371, 1354, 1289, 1272, 1203, 1156, 1106, 759, 742; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.25 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.69 (d, *J* = 9.2 Hz, 2H), 7.52 (s, 1H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.18-7.12 (m, 1H), 6.76 (t, *J* = 6.8 Hz, 1H), 2.38 (s, 3H), 1.70 (s, 9H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 148.7, 147.4, 138.3, 136.9 (2C), 129.8, 129.6 (3CH), 126.1 (2CH), 123.6, 117.8, 117.6, 117.5, 110.6, 85.0, 28.3 ($3CH_3$), 21.5 (CH_3). HRMS (ESI): for $C_{21}H_{22}N_3O_2$ $(M + H)^+$: *m/z* calcd. 348.1712, found 348.1707.

Tert-butyl 3-(4-fluorophenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate ***(5j)***. Yellow solid (128 mg, 49% yield); 181-183 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1728, 1519, 1505, 1372, 1354, 1156, 1109, 1061, 838, 759, 742; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.25 (d, *J* = 7.3 Hz, 1H), 8.08-7.04 (m, 2H), 7.70-7.67 (m, 1H), 7.50 (s, 1H), 7.20-7.11 (m, 3H), 6.78 (td, J_1= 6.9, J_2= 1.2 Hz, 1H), 1.71 (s, 9H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 162.2 d, *J* = 248 Hz), 148.6, 147.6, 138.2, 133.5, 128.9, 128.0 (d, *J* = 7.8 Hz, 2CH), 126.3, 123.8, 118.4, 117.9, 116.8, 115.8 (d, *J* = 21.6 Hz, 2CH), 110.7, 85.3, 28.3 ($3CH_3$); $^{19}F\{1H\}$ NMR (188 MHz, $CDCl_3$) *δ* -114.92; HRMS (ESI): for $C_{20}H_{19}N_3O_2F$ $(M + H)^+$: *m/z* calcd. 352.1461, found 352.1466.

*Tert-butyl 3-(3,4,5-trifluorophenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5k**)*. Yellow solid (117 mg, 60% yield); 180-182 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1734, 1524, 1433, 1370, 1333, 1287, 1246, 1154, 1109, 1043, 733; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.21 (d, *J* = 6.3 Hz, 1H), 7.72-7.65 (m, 3H), 7.46 (s, 1H), 7.21-7.16 (m, 1H), 6.79 (t, *J* = 6.8 Hz, 1H), 1.72 (s, 9H); ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ (ppm):151.1 (ddd, *J* = 249.7, 10.1, 4.0 Hz), 148.4, 147.8, 145.9 (d, *J* = 12 Hz), 138.7 (dd, *J* = 253, 15 Hz, 2C), 137.5, 129.0, 126.3, 124.1, 119.1, 117.9, 115.0,111.0, 110.2 (d, *J* = 22.0 Hz, 2CH), 85.8, 28.3 ($3CH_3$); ^{19}F{1H} NMR (188 MHz, $CDCl_3$) *δ* -134.44 (d, *J* = 20.5 Hz), -162.54 (t, *J* = 20.7 Hz); HRMS (ESI): for $C_{20}H_{17}F_3N_3O_2$ $(M + H)^+$: *m/z* calcd. 388.1273, found 388.1281.

*Tert-butyl 3-(4-chlorophenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5l**)*. Yellow solid (116 mg, 63% yield); mp 179-181 ºC; R_f = 0.4 (cyclohexane/ethyl acetate 5/5); IR (film, cm^{-1}): 1724, 1518, 1352, 1337, 1288, 1204, 1153, 1108, 1091, 1060, 834, 759, 741; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (d, *J* = 6.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 9.1 Hz, 1H), 7.54 (s, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.20-7.15 (m, 1H), 6.78 (t, *J* = 6.9 Hz, 1H), 1.71 (s, 9H). ^{13}C{1H} NMR (95 MHz, $CDCl_3$) δ (ppm): 148.6, 147.7, 143.2, 137.9, 132.8, 131.3, 129.1 (2CH), 127.6 (2CH), 126.3, 123.9, 118.7, 117.9, 116.6, 110.8, 85.4, 28.3 ($3CH_3$). HRMS (ESI): for $C_{20}H_{19}N_3O_2Cl$ $(M + H)^+$: *m/z* calcd. 368.1166, found 368.1166.

*Tert-butyl 3-(4-cyanophenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5m**)*. Yellow solid (152 mg, 85% yield); mp 294-296 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1731, 1608, 1518, 1372, 1354, 1291, 1202, 1155, 1110, 1061, 847, 744; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.20 (d, *J* = 6.6 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 2H), 7.69-7.60 (m, 4H), 7.21-7.16 (m, 1H), 6.79 (t, *J* = 6.9 Hz, 1H), 1.72 (s, 9H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 148.3, 147.8, 137.7, 137.5, 132.6 (2CH), 126.5 (2CH), 126.3, 124.2, 119.9, 119.3 (2C), 117.9, 115.7, 111.0, 110.1, 85.9, 28.3 ($3CH_3$). HRMS (ESI): for $C_{21}H_{19}N_4O_2$ $(M + H)^+$: *m/z* calcd. 359.1508, found 359.1512.

*Tert-butyl 3-([1,1'-biphenyl]-4-yl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5n**)*. Yellow solid (153 mg, yield 75%); mp 296-299 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1727, 1519, 1395, 1354, 1288, 1202, 1155, 1106, 1065, 847, 756, 743; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.25 (d, *J* = 6.0 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 2H), 7.73-7.60 (m, 6H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.37-7.32 (m, 1H), 7.19-7.14 (m, 1H), 6.77 (t, *J* = 6.8 Hz, 1H), 1.73 (s, 9H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 148.6, 147.6, 141.1, 139.9, 138.3, 131.8 (2C), 128.9 (2CH), 127.6 (2CH), 127.3, 127.1 (2CH), 126.7 (2CH), 126.2, 123.6, 118.6, 117.9, 117.3, 110.6, 85.2, 28.3 ($3CH_3$). HRMS (ESI): for $C_{26}H_{24}N_3O_2$ $(M + H)^+$: *m/z* calcd. 410.1869, found 410.1877.

*Tert-butyl 3-(pyridin-3-yl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5o**)*. Yellow solid (137 mg, 82% yield); mp 172-174 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1730, 1518, 1372, 1355, 1286, 1205, 1156, 1110, 760; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (d, *J* = 6.6 Hz, 1H), 9.18 (d, *J* = 6.6 Hz, 1H), 8.53 (dd, J_1 = 4.9C Hz, J_2 = 1.7 Hz, 1H), 8.49 (dt, J_1 = 7.9 Hz, J_2 = 2.0 Hz, 1H), 7.68 (d, *J* = 9.3 Hz, 1H), 7.61 (s, 1H), 7.37 (dd, J_1 = 7.9 Hz, J_2 = 4.8 Hz, 1H), 7.21-7.15 (m, 1H), 6.79 (t, *J* = 6.9 Hz, 1H), 1.72 (s, 9H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 148.5 (C), 148.2 (CH), 147.8 (C), 147.2 (CH), 139.9, 138.2, 133.9 (CH), 128.9 (C), 126.3 (CH), 124.0 (CH), 123.8 (CH), 118.9 (CH), 117.9 (CH), 114.4 (C), 110.8 (CH), 85.6 (C), 28.3 ($3CH_3$). HRMS (ESI): for $C_{19}H_{19}N_4O_2$ $(M + H)^+$: *m/z* calcd. 335.1508, found 335.1502.

*Tert-butyl 3-(9-methyl-9H-carbazol-3-yl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5p**)*. Yellow solid (135 mg, 62% yield); mp 198-200 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1726, 1519, 1352, 1336, 1246, 1151, 1107, 746, 726; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.29 (d, *J* = 5.8 Hz, 1H), 8.79 (s, 1H), 8.29-8.25 (m, 2H), 7.76 (d, *J* = 9.2 Hz, 1H), 7.63 (s, 1H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.28-7.16 (m, 2H), 6.79 (t, *J* = 6.9 Hz, 1H), 3.88 (s, 3H), 1.75 (s, 9H). $^{13}C\{1H\}$ NMR (101 MHz,

$CDCl_3$) δ (ppm): 148.9, 147.4, 141.6 (2C), 140.6 (2C), 126.3, 125.9, 124.8, 123.7, 123.6, 123.4, 123.1, 121.0, 119.0, 118.7, 118.1, 117.9, 117.7, 110.7, 108.8, 108.6, 85.0, 29.3 (NCH_3), 28.4 ($3CH_3$). HRMS (ESI): for $C_{27}H_{25}N_4O_2$ $(M + H)^+$: *m/z* calcd. 437.1978, found 437.1977.

Tert-butyl 5H-benzo[e]pyrido[2',1':2,3]imidazo[4,5-b]indole-7(6H)-carboxylate (***5q***). Yellow solid (120 mg, 67 % yield); mp 187-189 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}):1758, 1721, 1515, 1370, 1351, 1283, 1247, 1153, 1132, 1115, 1066, 763, 733; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (d, *J* = 7.1 Hz, 1H), 8.18 (d, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 9.2 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.19-7.10 (m, 3H), 6.74 (t, *J* = 6.9 Hz, 1H), 3.30 (t, *J* = 7.9 Hz, 2H), 3.11 (t, *J* = 8.0 Hz, 2H), 1.70 (s, 9H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.8, 147.6, 136.9, 134.1, 132.9 (2C), 130.98, 127.3, 127.0, 126.4, 126.2, 124.9, 123.0, 117.8, 113.5, 110.5, 85.4, 29.4, 28.4 ($3CH_3$), 24.2 (CH_2). HRMS (ESI): for $C_{22}H_{22}N_3O_2$ $(M + H)^+$: *m/z* calcd. 360.1712, found 360.1716.

Tert-butylthiochromeno[4'',3'':4',5']pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-7(6H)-carboxylate (***5r***). Yellow solid (156 mg, 82% yield); mp 143-145 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1730, 1516, 1423, 1371, 1352, 1330, 1280, 1258, 1154, 1117, 760, 736; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.30 (d, *J* = 6.9 Hz, 1H), 8.41 (d, *J* = 7.5 Hz, 1H), 7.78 (d, *J* = 9.1 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.25 (q, *J* = 6.6 Hz, 2H), 6.86 (t, *J* = 6.7 Hz, 1H), 4.60 (s, 2H), 1.81 (s, 9H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 149.5, 147.8, 143.8, 139.6, 136.7, 129.8, 128.5, 127.3, 127.1, 126.8, 126.5 (2CH), 126.4, 123.6, 117.9, 110.8, 86.5, 28.4 ($3CH_3$), 25.7 (SCH_2). HRMS (ESI): for $C_{21}H_{20}N_3O_2S$ $(M + H)^+$: *m/z* calcd. 378.1276, found 378.1268.

Tert-butyl chromeno[4'',3'':4',5']pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-7(6H)-carboxylate (***5s***). Yellow solid (130 mg, 72% yield); mp 179-181 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1730, 1515, 1372, 1355, 1325, 1156, 1067, 1039, 861, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.23 (d, *J* = 6.8 Hz, 1H), 7.99 (d, *J* = 8.3

Hz, 1H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.20-7.12 (m, 2H), 7.06-7.01 (m, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 6.78 (t, *J* = 6.9 Hz, 1H), 5.67 (s, 2H), 1.70 (s, 9H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 153.4, 149.5, 148.6, 147.9, 131.3, 128.2, 126.3, 125.2, 123.7, 122.2, 119.1, 118.7, 118.0, 115.7, 111.7, 110.9, 86.4, 65.4 (OCH_2), 28.3 ($3CH_3$). HRMS (ESI): for $C_{21}H_{20}N_3O_3$ $(M + H)^+$: *m/z* calcd. 362.1505, found 362.1508.

*Tert-butyl2,3-bis(4-methoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5t**).* Yellow solid (305 mg, 65% yield); mp 196-197 ºC; R_f = 0.35 (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1718, 1515, 1355, 1326, 1198, 1178, 1152, 1099, 1072, 744; ^1H NMR (300 MHz, $CDCl_3$) *δ* (ppm): 9.24 (d, *J* = 7.7 Hz, 1H), 7.67 (d, *J* = 9.8 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.15– 7.10 (m, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.74 (t, *J* = 6.9 Hz, 1H), 3.84 (s, 3H), 3.75 (s, 3H), 1.24 (s, 9H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) *δ* (ppm): 159.6, 158.3, 150.1, 147.3, 138.5, 132.5 (2CH), 132.3, 129.9 (2CH), 126.9,126.4 125.6, 124.8, 123.2, 117.7, 116.6, 113.8 (2CH), 113.8 (2CH), 110.4, 84.3, 55.5, 55.2, 27.6 ($3CH_3$); HRMS (ESI): for $C_{28}H_{28}N_3O_4$ $(M + H)^+$: *m/z* calcd. 470.2080, found 470.2056.

*Tert-butyl 3-(4-methoxyphenyl)-7-(4-(trifluoromethyl)phenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5u**).* Yellow solid (156 mg, 62% yield); mp 298-299 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1728, 1616, 1510, 1390, 1326, 1295, 1252, 1178, 1161, 1125, 1070, 834; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.06 (s, 1H), 7.56-7.52 (m, 2H), 7.29-7.26 (m, 5H), 7.00 (s, 1H), 6.93 (dd, J_1 = 9.5, J_2 = 2.0 Hz, 1H). 6.54-6.50 (m, 2H), 3.38 (s, 3H), 1.24 (s, 9H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 159.1, 146.7 (2C), 143.0, 141.6 (d, *J* = 27 Hz), 129.9, 127.6 (3CH), 127.4 (2CH), 126.1 (q, *J* = 15 Hz, 2CH), 125.5 (d, *J* = 270 Hz), 125.2 (2C), 123.5, 122.5, 119.8, 117.9, 116.2, 114.5 (2CH), 84.2, 55.5 (OCH_3), 25.3 ($3CH_3$); $^{19}F\{1H\}$ NMR (188 MHz, $CDCl_3$) *δ* -62.50; HRMS (ESI): for $C_{28}H_{25}F_3N_3O_3$ $(M + H)^+$: *m/z* calcd. 508.1848, found 508.1843.

*Tert-butyl 3,7-bis(4-methoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5v**)*. Yellow solid (128 mg, 55% yield); mp 282-284 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1723, 1508, 1390, 1348, 1282, 1244, 1178, 1159, 1125, 1067, 833; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.42 (s, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.72 (d, *J* = 9.5 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.48 (s, 1H), 7.40 (d, *J* = 9.5 Hz, 1H), 7.05-6.96 (m, 4H), 3.86 (m, 6H), 1.71 (s, 9H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 159.4, 159.0, 156.9, 148.7, 146.7, 130.6 (2C), 130.2, 128.2 (3CH), 127.6 (2CH), 125.4 (2C), 124.3, 117.5, 117.4, 114.6 (2CH), 114.4 (2CH), 85.3, 55.5 (OCH_3), 55.4 (OCH_3), 28.3 ($3CH_3$). HRMS (ESI): for $C_{28}H_{28}N_3O_4$ $(M + H)^+$: *m/z* calcd. 470.2080, found 470.2090.

*Tert-butyl 3-(4-methoxyphenyl)-7-phenyl-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5w**)*. Yellow solid (132 mg, 60% yield); mp 274-276 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 8/2); IR (film, cm^{-1}): 1722, 1510, 1393, 1349, 1244, 1178, 1158, 1124, 1066, 833, 755; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.31 (s, 1H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 9.5 Hz, 1H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.33-7.20 (m, 5H), 6.85 (d, *J* = 8.6 Hz, 2H), 3.70 (s, 3H), 1.58 (s, 9H); $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 158.8, 148.5, 146.6, 137.9 (2C), 129.1, 129.0 (2CH), 127.5, 127.4 (2CH), 127.0 (2CH), 126.7, 125.3 (2C), 124.7, 124.0, 117.4, 117.2, 114.2 (2CH), 84.1, 55.3 (OCH_3), 28.2 ($3CH_3$). HRMS (ESI): for $C_{27}H_{26}N_3O_3$ $(M + H)^+$: *m/z* calcd. 440.1974, found 440.1964.

*Tert-butyl 3-(4-methoxyphenyl)-7-(1-(4-methoxyphenyl)vinyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-1-carboxylate (**5x**)*. Yellow solid (143 mg, 58% yield); mp 153-155 ºC; R_f = 0.3 (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1724, 1608, 1511, 1393, 1347, 1248, 1179, 1154, 1108, 1032, 835; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.25 (s, 1H), 8.02 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 9.5 Hz, 1H), 7.51 (s, 1H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 9.4 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.48 (s, 1H), 5.45 (s, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 1.64 (s, 9H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ

(ppm): 159.8 (2C), 159.0 (2C), 148.6, 147.0, 146.2 (2C), 133.1, 129.4 (2CH), 127.6 (2CH), 125.8, 125.4, 125.2, 124.6, 118.0, 117.4, 116.8, 114.4 (2CH), 113.9 (2CH), 113.4, 85.2, 55.5 (OCH_3), 28.3 ($3CH_3$). HRMS (ESI): for $C_{30}H_{30}N_3O_4$ $(M + H)^+$: *m/z* calcd. 496.2236, found 496.2241.

*Tert-butyl 10-(3,4-dihydronaphthalen-1-yl)-5H-benzo[e]pyrido[2',1':2,3]imidazo[4,5-b]indole-7(6H)-carboxylate (**5y**).* Yellow solid (321.8 mg, 66% yield); mp 206-207 ºC; $R_f = 0.4$ (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1722, 1512, 1392, 1371, 1347, 1301, 1282, 1260, 1156, 1136, 765; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.24 (s, 1H), 8.21 (d, $J = 7.5$ Hz, 1H), 7.68 (d, $J = 9.4$ Hz, 1H), 7.34 (t, $J = 7.9$ Hz, 1H), 7.23-7.11 (m, 6H), 7.04 (d, $J = 7.0$ Hz, 1H), 6.22 (t, $J = 4.6$ Hz, 1H), 3.34 (t, $J = 8.0$ Hz, 2H), 3.13 (t, $J = 7.9$ Hz, 2H), 2.90 (t, $J = 7.9$ Hz, 2H), 2.50-2.44 (m, 2H), 1.67 (s, 9H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): 149.6, 147.1, 137.2, 136.7 (2C), 134.8, 134.4, 132.9 (2C), 130.9, 128.7, 127.8, 127.4, 127.4, 127.1, 126.5, 126.4, 125.4, 125.3, 124.9, 124.6, 124.3, 116.7, 113.6, 85.5, 29.4, 28.4 ($3CH_3$), 28.3, 24.2, 23.6; HRMS (ESI): for $C_{32}H_{30}N_3O_2$ $(M + H)^+$: *m/z* calcd. 488.2338, found 488.2344.

*Tert-butyl 10-(2H-chromen-4-yl)chromeno[4'',3'':4',5']pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine-7(6H)-carboxylate (**5z**).* Yellow solid (329 mg, 67% yield); mp 202-203 ºC; $R_f = 0.3$ (cyclohexane/ethyl acetate 7/3); IR (film, cm^{-1}): 1730, 1447, 1356, 1330, 1315, 1290, 1065, 764, 748; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.28 (s, 1H), 8.02 (d, $J = 7.2$ Hz, 1H), 7.71 (d, $J = 9.6$ Hz, 1H), 7.25-7.12 (m, 3H), 7.07 (ddt, $J = 9.2, 7.7, 1.4$ Hz, 2H), 6.92 (ddd, $J = 10.2, 7.7, 6.3$ Hz, 3H), 5.96 (t, $J = 3.9$ Hz, 1H), 5.71 (s, 2H), 4.93 (d, $J = 3.7$ Hz, 2H), 1.69 (s, 9H); $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ (ppm): $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 154.7, 151.5, 148.7, 147.1, 136.3, 133.9 (2C), 129.7 (2CH), 128.1, 125.6, 125.1, 125.1, 123.1, 122.2 (2C), 122.1, 121.4, 120.9, 119.0, 117.1, 116.4, 115.6, 109.7, 86.4, 65.2 ($2CH_2$), 28.15 ($3CH_3$). HRMS (ESI): for $C_{30}H_{26}N_3O_4$ (M + H)+: *m*/z calcd. 492.1923, found 492.1920.

General procedure to prepare compounds 5aa, 5cc, 5gg, and 5kk. In a 5 mL microwave reaction vial, compound **5a**, **5c**, **5g**, or **5k** (0.1 mmol, 1 equiv.) was dissolved in methanol and water (1:2 V/V) and trifluoroacetic acid (*ca*. 1 mg) was added to a solution. The reaction

mixture was subjected to microwave irradiation with stirring at 100 °C for 30 minutes. After the system had cooled down to room temperature, the reaction was diluted with H_2O, and extracted with ethyl acetate. The organic layer was washed with H_2O and brine and dried with Na_2SO_4, and the solvents were evaporated to give compounds **5aa**, **5cc**, **5gg** and **5kk** in excellent yields.

*3-Phenyl-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine (**5aa**)*. Yellow solid (23 mg, 98% yield); mp 247-249 ºC; IR (film, cm^{-1}): 1675, 1605, 1512, 1221, 1203, 846, 802, 755, 739, 724, 694; ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 11.70 (s, 1H), 8.47 (d, *J* = 6.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.62-7.57 (m, 2H), 7.38 (t, *J* = 7.7 Hz, 14, 2H), 7.20-7.11 (m, 2H), 6.87 (t, *J* = 6.3 Hz, 1H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 145.0, 135.1, 134.5, 128.5 (2CH), 125.9, 124.8, 124.6 (2CH), 123.1, 122.2, 118.3, 116.9, 110.5, 109.8; HRMS (ESI): for $C_{15}H_{12}N_3$ $(M + H)^+$: *m/z* calcd. 234.1031, found 234.1036.

*3-(Phenanthren-3-yl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine (**5cc**)*. Yellow solid (32 mg, 96% yield); mp 259-261 ºC; IR (film, cm^{-1}): 1511, 1496, 1341, 1302, 1261, 1221, 844, 804, 753, 736; ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 11.73 (s, 1H), 9.47 (s, 1H), 9.83 (d, *J* = 7.9 Hz, 1H), 8.47 (d, *J* = 6.8 Hz, 1H), 8.40-8.35 (m, 1H), 8.02-7.96 (m, 3H), 7.75-7.61 (m, 5H), 7.24-7.16 (m, 1H), 6.92 (t, *J* = 6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): ^{13}C NMR{1H} (75 MHz, $CDCl_3$) δ 145.2, 134.9, 133.9, 131.9, 130.2, 129.7, 129.3, 128.7, 128.5, 126.7, 126.7, 126.5, 126.1, 125.3, 124.2, 123.0, 122.8, 122.3, 119.3, 117.5, 117.1, 110.8, 109.9; HRMS (ESI): for $C_{23}H_{16}N_3$ $(M + H)^+$: *m/z* calcd. 334.1344, found 334.1339.

*3-(3,5-Dimethoxyphenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine (**5gg**)*. Yellow oil (27 mg, 92% yield); IR (film, cm^{-1}): 1607, 1589, 1511, 1457, 1339, 1203, 1154, 1063, 842, 768, 740; ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 11.57 (s, 1H), 8.41 (d, *J* = 7.5 Hz, 1H), 7.65-7.57 (m, 2H), 7.25 (d, *J* = 2.0 Hz, 2H), 7.19-7.10 (m, 1H), 6.87 (t, *J* = 7.0 Hz, 1H), 6.32-6.31 (m, 1H), 3.81 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7

(2C), 145.0 (C), 136.9 (C), 134.7, 125.8 (C), 122.9 (CH), 122.1 (CH), 118.9 (CH), 117.0 (CH), 116.0 (C),109.8 (CH), 102.9 (2CH), 97.0 (CH), 55.1 (2OCH_3); HRMS (ESI): for $C_{17}H_{16}N_3O_2$ $(M + H)^+$: *m/z* calcd. 294.1243, found 294.1241.

*3-(3,4,5-Trifluorophenyl)-1H-pyrrolo[3',2':4,5]imidazo[1,2-a]pyridine (**5kk**).* Yellow solid (25 mg, 88% yield); mp 262-265 ºC; IR (film, cm^{-1}): 1554, 1528, 1436, 1361, 1340, 1252, 1205, 1049, 1025, 1006, 762, 737. ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 11.92 (s, 1H); 8.48 (d, *J* = 6.7 Hz, 1H), 7.95-7.87 (m, 2H), 7.75 (s, 1H), 7.61 (d, *J* = 9.4 Hz, 1H), 7.22-7.14 (m, 1H), 6.89 (t, *J* = 6.7 Hz, 1H); ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 150.7 (dt, *J* = 250, 10 Hz, 2C), 145.4, 140.5 (d, *J* = 43 Hz), 134.4, 132.4 (d, *J* = 35 Hz), 127.4 (dt, *J* = 253, 15 Hz), 125.9, 123.2, 122.6, 199.8, 117.0, 110.1, 108.2 (d, *J* = 20.9 Hz, 2CH); ^{19}F{1H} NMR (188 MHz, $CDCl_3$) *δ* -136.18 (d, *J* = 21.8 Hz), -167.26 (t, *J* = 21.7 Hz); HRMS (ESI): for $C_{15}H_9F_3N_3$ $(M + H)^+$: *m/z* calcd. 288.0749, found 288.0748.

General procedure for the one-pot cross-coupling between *N*-tosylhydrazones 1 and 2-chloro-3-nitroimidazo[1,2-*a*]pyridine 2. A 10 mL sealed tube under argon atmosphere was charged with *N*-tosylhydrazone (1.0 mmol, 1.0 equiv), 2-chloro-3-nitroimidazo[1,2-*a*]pyridine (1.0 mmol, 1.0 equiv.), Pd_2dba_3·$CHCl_3$ (2.5 mol %), and XPhos (5 mol %) in dioxane (4.0 mL), and the mixture was stirred at room temperature for 1 minute before the addition of LiO*t*Bu (2.2 mmol, 2.2 equiv.). Then the tube was put into microwave and stirred at 110 °C for 30 minutes. Then $MoO_2Cl_2(dmf)_2$ (10 mol%), PPh_3 (4 equiv), were added, and the mixture was irradiated at 135 °C for 4 h. Finally, $(Boc)_2O$ (1.3 mmol), DMAP (0.2 mmol), TEA (3 mmol), were added and the mixture was stirred at rt for 2 h. After cooling to r.t., DCM was added to the mixture. The solvents were evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel using cyclohexane and ethyl acetate (7:3 to 3:7) as eluent to afford the desired product.

Biology

Cell culture and proliferation assays. HCT116 cancer cell line was obtained from the American type Culture Collection (ATCC, Rockville, MD) and was cultured according to the supplier's instructions. Human HCT116 colorectal carcinoma were grown in Gibco McCoy's 5A supplemented with 10% fetal calf serum (FCS) and 1% glutamine and were maintained at 37°C in a humidified atmosphere containing 5% CO_2. Cell viability was determined by a luminescent assay according to the manufacturer's instructions (Promega, Madison, WI, USA).

For IC_{50} determination, the cells were seeded in 96-well plates (3×10^3 cells/well) containing 100 μL of growth medium. After 24 h of culture, the cells were treated with the tested compounds at 10 different final concentrations. Each concentration was obtained from serial dilutions in culture medium starting from the stock solution. Control cells were treated with the vehicle. Experiments were performed in triplicate. After 72 h of incubation, 100 μL of CellTiter Glo Reagent was added for 15 min before recording luminescence with a spectrophotometric plate reader Polar Star Omega (BMG LabTech). The dose-response curves were plotted with Graph Prism software and the IC_{50} values were calculated using the Graph Prism software from polynomial curves (four or five-parameter logistic equations). IC_{50} values correspond to the concentration of test compound that causes a 50% decrease in fluorescence of drug-treated cells relative to untreated cells. Experiments were performed in triplicate. IC_{50} values for all compounds were compared with this CA-4 and were measured the same day under the same conditions.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org

- Copies of ^1H and ^{13}C NMR spectra (PDF), X-ray data figures
- X-ray crystal structure for compound **5e** (CCDC 1920290) (CIF)
- X-ray crystal structure for compound **5s** (CCDC 1942283) (CIF)

- X-ray crystal structure for compound **5u** (CCDC 1942284) (CIF)

AKNOWLEDGMENT

K. Zhang thanks the Chinese Scholarship Council for Ph.D. funding. The authors gratefully acknowledge support of this project by CNRS, University Paris-Sud and "La Ligue Contre le Cancer" throughout an "Equipe Labellisée 2014" grant. Our laboratory (Biocis UMR 8076 is a member of the laboratory of excellence LERMIT supported by a grant from ANR (ANR-10-LABX-33).

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