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N-Amino-7-Azaindole as N,N'- Bidentate Directing Group: Ruthenium-Catalyzed Oxidative Annulation of N-(7-Azaindole) Benzamides with Alkynes via C-H Bond Activation

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N-Amino-7-Azaindole as *N,N'*- Bidentate Directing Group: Ruthenium-Catalyzed Oxidative Annulation of *N*-(7-Azaindole) Benzamides with Alkynes *via* C-H Bond Activation

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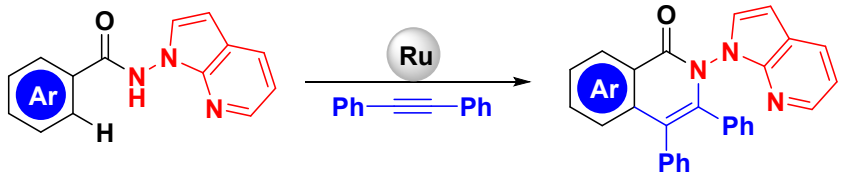


25 examples
Up to 85% yield

ABSTRACT: We report a new application of *N*-amino-7-azaindole as a new bidentate directing group for [Ru(*p*-cymene)Cl_2]$_2$-catalyzed C(sp^2)-H alkenylation/annulation of *N*-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamides with internal alkynes to afford *N*-isoquinolono-7-azaindole *via* the formation of C-C and C-N bond. The reaction shows a wide range of substrate scope with different symmetrical and unsymmetrical alkynes affording the desired product in good to excellent yields. In the case of unsymmetrical alkynes a highly regioselective product was obtained, which was confirmed by single crystal X-ray Crystallography. A new ruthenium-4-methyl-*N*-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide complex was isolated and its structure was confirmed by single crystal X-ray Crystallography.

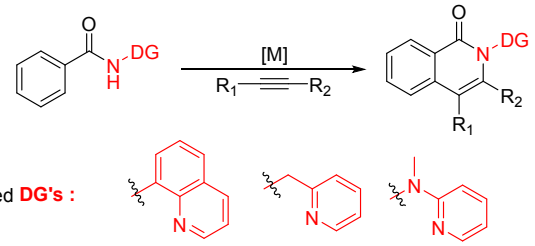
INTRODUCTION

Directing group assisted transition-metal-catalysed C-H activation and annulation reaction has been utilized for the synthesis of numerous biologically important molecular scaffolds such as isoquinolines,[1] isoquinolones, [2] pyridines,[3] and indoles[4] etc. Ever since the discovery of 8-aminoquinoline as a directing group for C-H activation reactions by Dauglis et al. in the year 2005,[5] it has become the most successful and widely used directing group for C-H activation reactions.[6] The rigidity of its structure, ionic and hemilabile neutral nitrogen binding modes are just the right combination required for C-H activation reactions. One major draw-back on the use of this directing group for C-H/N-H annulation type of reaction is that isoquinoline

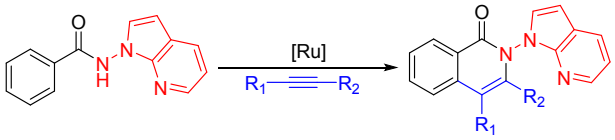
unit cannot be removed from the substrate easily from the reaction due to the presence of strong C-N bond,[7] this reduces its scope for further modification of the products. The 5-methoxy-8-aminoquinolines were demonstrated to solve this problem, however it is very rarely used.[8] There are several reports for C-H activation reactions utilizing N-O bond containing directing group which would also act as an internal oxidant.[9] However, the N-N bond containing directing groups are not well explored for C-H activation. Therefore, we started a new program in our group to discover new N-N bond containing directing groups for C-H activation reaction wherein directing group could be easily cleaved for further synthetic modification of the product. We designed and developed *N*-amino-7-azaindole as a new substitute for 8-aminoquinoline, wherein the azaindole unit can be removed easily after the reaction using hydrazine. To the best of our knowledge, this is the first report of N-N bond cleavage using hydrazine. The procedure is very simple and mild as compared to the methods reported in the literature.[10] The details of this new N-N bond cleavage process is explained in the later part of this article. Although C-H alkenylation/annulation reaction is well documented in the literature.[11] It is worth mentioning that *N*-amino-7-azaindole derivatives as *N,N*'-bidentate directing group were not explored in previous reports. Moreover, the bidentate auxiliary containing N-N bond linkage seems to be rare and helpful for easy removal as compared to the C-N counterpart (Scheme 1).[12]

Scheme 1. Overview of this work

(a) Previous work: Various bidentate direction groups for isoquinolone synthesis.[11a, b, 12b]



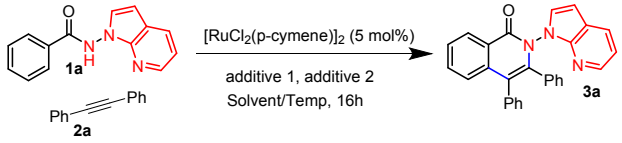
(b) **Our work:** Ru(II)-catalyzed annulation of alkyne *via* C-H activation.



RESULTS AND DISCUSSION

N-amination of 7-azaindole can be easily performed using monochloramine as NH_2^+ transfer reagent using the procedure reported by Hynes et al.[13] Since ruthenium (II) is known to activate *ortho* C(*sp*²)-H bond of benzamides, we have taken *N*-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**1a**) as a model substrate for the annulation purpose. For screening, we decided to use the commercially available $[Ru(p\text{-cymene})Cl_2]_2$ catalyst for the synthesis of N-N bonded isoquinolone derivatives of 7-azaindoles using diphenyl acetylene as coupling partner.[14]

Table 1: Optimization of reaction conditions[a,b]



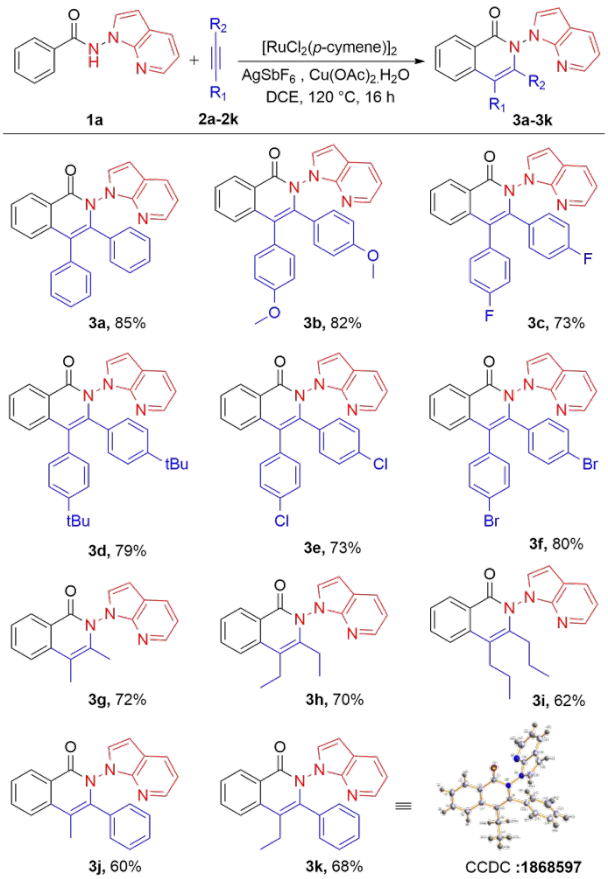
entry	additive-1	additive-2	solvent/temp (°C)	Yield [b] (%)
1	-	NaOAc	MeOH/100	30
2	PivOH	CsOAc	MeOH/120	30
3	MesCOOH	KOAc	H_2O /100	50
4	MesCOOH	KOAc	TFE/100	60
5	MesCOOH	$Cu(OAc)_2.H_2O$	TFE/100	65
6	MesCOOH	KOAc	PEG-400/100	15
7	MesCOOH	KOAc	DCE/120	45
8	-	CsOAc	DCE/120	40
9	$AgSbF_6$	-	DCE/120	25
10	-	$Cu(OAc)_2.H_2O$	DCE/120	50
11[c]	$AgSbF_6$	$Cu(OAc)_2.H_2O$	DCE/120	28
12[d]	$AgSbF_6$	$Cu(OAc)_2.H_2O$	DCE/120	34
13[e]	$AgSbF_6$	$Cu(OAc)_2.H_2O$	DCE/120	42
14[f]	$AgSbF_6$	$Cu(OAc)_2.H_2O$	DCE/120	60
15[g]	**$AgSbF_6$**	**$Cu(OAc)_2.H_2O$**	**DCE/120**	**85**
16[h]	**-**	-	DCE/120	trace

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1.2 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (5.0 mol %), Additive 1 (10 mol %), Additive 2 (2.0 equiv), solvent (3.0 mL), 100 – 120 °C, 16h. [b] Isolated Yield. [c] $Cu(OAc)_2.H_2O$ (10mol%), [d]$Cu(OAc)_2.H_2O$ (30mol%), [e]$Cu(OAc)_2.H_2O$ (50mol%), [f]$Cu(OAc)_2.H_2O$ (100mol%), [g] $Cu(OAc)_2.H_2O$ (200 mol%), [h] without additives.

By keeping the time constant we explored various acetates, acids, solvents at different temperatures (Table 1, entry 1-8), but the yields of **3a** were not promising. It has been observed in the literature that silver salts such as $AgSbF_6$ is known to improve the reaction yields. Therefore we decided to screen various combinations of $AgSbF_6$ and $Cu(OAc)_2.H_2O$ as additives. When the reaction was performed only with $AgSbF_6$ in 1,2 dichloroethane as solvent we obtained **3a** in 25% isolated yield (Table 1, entry 9). Similarly, in presence of only $Cu(OAc)_2.H_2O$, **3a** was obtained in 50% yield (Table 1, entry 10). Then, we decided to use both the additives together by changing the $Cu(OAc)_2.H_2O$ percentage gradually as following; 10 mol %, 30 mol %, 50 mol %, 100 mol % and 200 mol % affording the product

yields 28%, 34%, 42%, 60%, and 85% respectively (Table 1, entry 11-15). It is very clear that by increasing the equivalent amount of copper salt the product yield also gradually increased. These preliminary experiments highlighted $[RuCl_2(p\text{-cymene})]_2$ /$AgSbF_6$/$Cu(OAc)_2.H_2O$ (Table S1, entry 15) as the best catalyst system and DCE was the most suitable among the solvents used. Herein, we demonstrate an efficient ruthenium-catalyzed cyclization of *N*-(7-azaindole) benzamides **1a** with alkynes **2a** to give isoquinolones in very good yields. With the optimized conditions in hand, we examined the scope of the alkynes with *N*-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide **1a**, as shown in Scheme 2. Screening of symmetrically substituted diaryl alkynes having methoxy, *t*-butyl and halogen groups at the para- position gave the products **3b–f** in 73 – 82% yields. The use of terminal alkynes gave no corresponding product. Whereas the symmetrical alkynes bearing aliphatic groups like 2-butyne, 3-hexyne, 4-octyne gave the corresponding product **3g–i** in 62%–72% yields. Interestingly, when unsymmetrical alkynes such as phenyl(alkyl)alkynes was used only one regioselective isomer was obtained. *viz* 1-phenyl-1-propyne **2j**, and 1-phenyl-1-butyne **2k** afforded the products in in good yields 60% & 68%. **3j** and **3k** respectively. The regioselective product **3k** was further confirmed by X-ray crystallography.

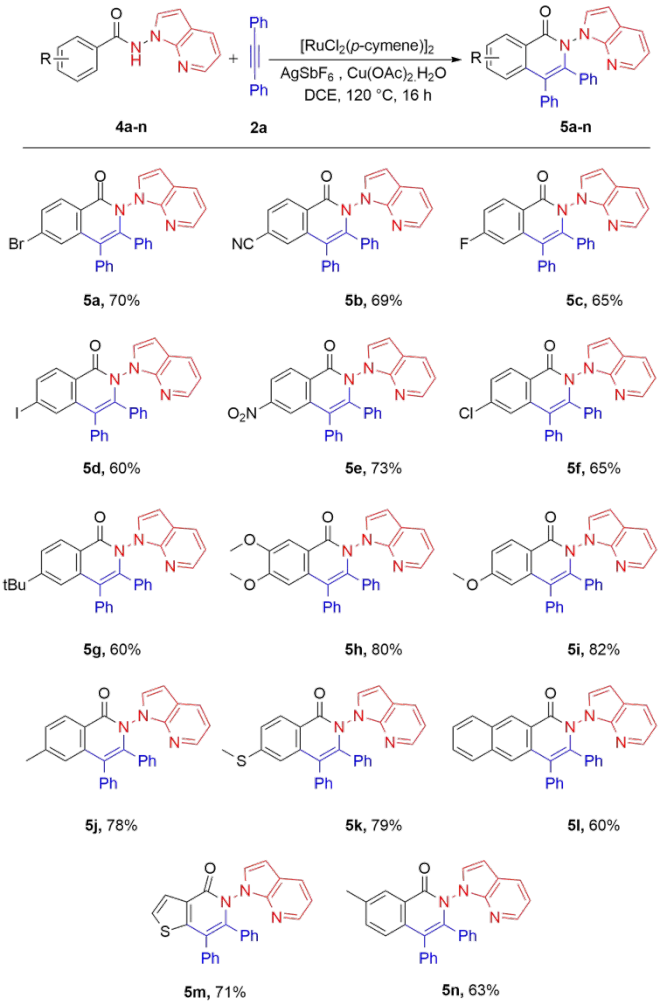
Scheme 2. Substrate scope for the various alkynes [a, b]



[a]Reaction conditions: All reactions were performed with **1a** (0.5 mmol), **2** (0.75 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (5.0 mol %), $AgSbF_6$ (10 mol %), and $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol) in 2.0 mL of DCE at 120 °C, 16 h in sealed tube. [b]isolated yields

We have also explored scope of various substituted *N*-(7-azaindole)benzamides (Scheme 3). The generality of the annulation reactions were explored using benzamides containing various functional groups **4a-n** with **2a** under optimized reaction conditions. The reactions are successful for both electron poor **4a–f** and electron rich **4g–k** amides. Therefore, the substituted benzamides **4a–n** with diphenylacetylene **2a** behaved similarly to afford the isoquinolones **5a–n** in good yields 60%–70%. The reaction also worked well with 2-naphtahylamide affording the product **5l** 60% yield. Extension of the annulation process to heteroarylamide, 3-thiopheneamide worked smoothly under catalytic conditions and gave the annulation product **5m,** (71%) in a regioselective manner.

Scheme 3. Substrate scope for the various benzamides [a, b]

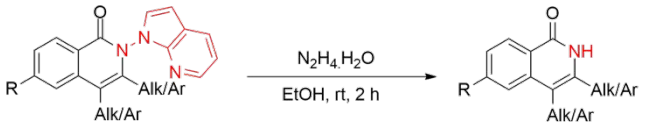


[a]All reactions were performed with **4** (0.5 mmol), **2a** (0.75 mmol), [Ru]-catalyst (0.025 mmol), $AgSbF_6$ (0.05 mmol), and $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol) in 2.0 mL DCE at 120 °C, 16 h in sealed tube. [b]isolated yields.

It is worth noticing that the C-H bond functionalization was occurred at the more active 2–position of the thiophene. When we used a meta-substituted Benzamides **4n** with diphenyacetylene **2a** we got the product **5n** as a single regioisomer in which the less hindered C-H bond got activated. The utility of directing group has to be tested for its easy removal, 8-aminoquinoline is a popular and very successful directing group employed in C-H activation reactions, but removal of quinoline moiety from the cyclized product is not very easy. However, in the case of *N*-amino-7-azaindole, it has the same directing group ability as 8-aminoquinoline but removal is very easy. For instance, compound **3a** when treated with $N_2H_4.H_2O$ in the presence of ethanol at room temperature for 2h, yielded the corresponding amide **3aa**[13] in 80% yield through N-N bond cleavage (Scheme 4). The same condition

was implemented for the cleavage of N-N bond of the other substituted 7-azaindole Isoquinolones **3g** & **5k** and obtained the corresponding isoquinolones **3gg** & **5kk** in excellent yields (Scheme 4).

Scheme 4. Directing group removal.

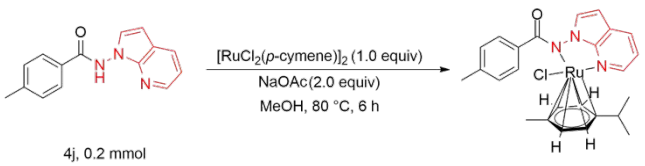


3a, 3g, & 5k **3aa, 3gg & 5kk, 80-82%**

entry	R	Alk/Ar	Yield (%)
1	H	Ph	80 (**3aa**)
2	H	CH_3	79 (**3gg**)
3	SCH_3	Ph	82 (**5kk**)

This methodology in itself is a newly discovered reaction and it was never reported before. As compared to literature methods for the cleavage of N-N bonds, by far this is the most-simple approach for the cleavage of N-N bonds. We also performed a stoichiometric reaction and isolated the intermediate ruthenium complex with the substituted benzamide (Scheme 5). The complex-**4j'** was obtained by treating the 4-methyl-*N*-(1H-pyrrolo[2,3-b]pyridin-1yl)benzamide **4j** with [Ru(*p*-cymene)Cl_2]$_2$ in 40% yield. In this complex, ruthenium is coordinated to the 4-methyl-*N*-(1H-pyr rolo[2,3-b]pyridin-1-yl)benzamide **4j** moiety in a *N,N* fashion.

Scheme 5. Synthesis of the ruthenium complex – 4j'.

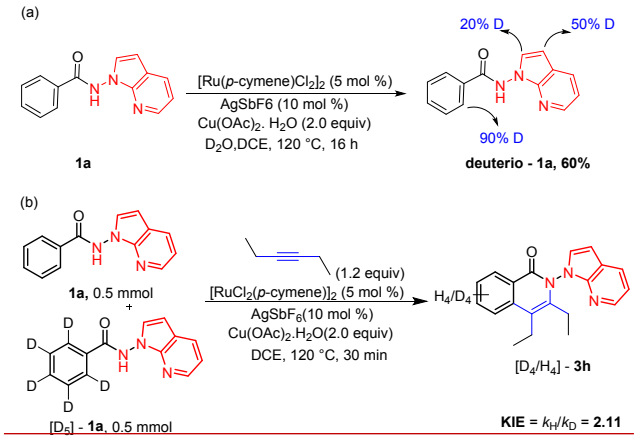


4j, 0.2 mmol Complex- 4j', 40%

The structure of the complex-**4j'** was further confirmed by X-ray crystallography (**CCDC: 1913752**). To have an insight into the reaction mechanism, a few mechanistic study experiments were conducted (Scheme 6). In the reaction **1a** with D_2O under the optimized condition using DCE as a solvent, the *ortho*- hydrogen of amide and C-2 and C-3 hydrogens of 7-azaindole were deuterated and obtained deuterio-**1a** in 60% yield with 90%, 20%, and

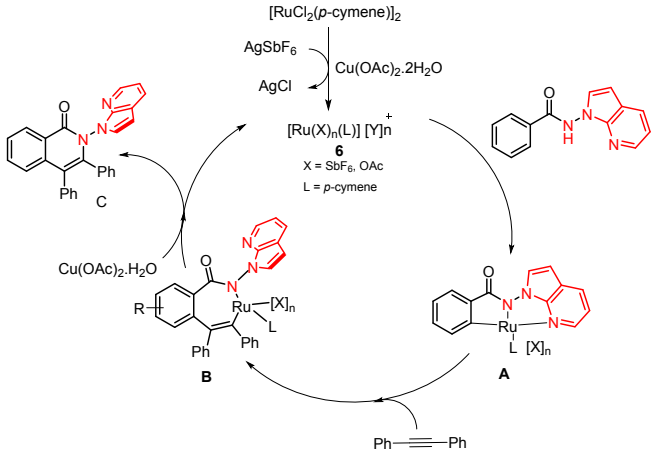
50% of deuterium incorporation respectively. Meanwhile, the intramolecular reaction involving **1a** / [D_5]-**1a** with 3-Hexyne showed the KIE value of 2.11, indicating that the C-H activating step might be turnover limiting step.

Scheme 6. Preliminary mechanistic studies. a) Deuterium exchange and b) Kinetic isotopic effect.



Based on the above mechanistic information and precedent reports[15] a plausible mechanism is proposed (Scheme 7). Firstly, the $AgSbF_6$ removes the chloro (Cl^-) ligand form the Ruthenium complex in the presence of the $Cu(OAc)_2.H_2O$ and gives a cationic ruthenium acetate complex **6.** Which in turn coordinate with the benzamide **1a** forms a five membered ruthenacycle intermediate **A**. The coordinative insertion of diphenyl acetylene into the Ru-carbon bond of the complex **A** gives the intermediate **B**. Finally, Reductive elimination of the intermediate **B** in the presence of Copper salt gives the desired product **C** and finally active ruthenium complex **6** regenerates for the next catalyst cycle.

Scheme 7. Proposed mechanism for the Ruthenium catalyzed Isoquinolone synthesis via bidentate directing group



CONCLUSIONS

In summary, we have developed a novel and efficient ruthenium–catalysed *ortho*-C(sp^2)-H functionalization and alkenylation/annulation of benzamides with internal alkynes via a novel *N*-amino-7-azaindole- assisted C-H activation. This protocol provides access to a series of *N*-isoquinolono-7-azaindole in good to excellent yields. Moreover, the isoquinoline unit of 7-azaindole directing group can be further removed using hydrazine under mild conditions, which is also a newly discovered reaction for N-N bond cleavage. The reaction features a high regioselectivity and good substrate scope. A ruthenium 4-methyl-*N*-(2,3-b)pyrrolo[2,3-b]pyridin-1-yl)benzamide complex was isolated and characterized, showing the key role played by the 7-Azaindole moiety. Further applications of *N*-amino-7-azaindole as a bidentate directing group in the other types of C-H functionalization and mechanistic details are currently being investigated in our laboratory.

EXPERIMENTAL SECTION

All the chemical reagents were purchased from commercial suppliers and used without further purification. Solvents were distilled and stored in the presence of 4 Å molecular sieves prior to use. Thin layer chromatography was carried out on aluminum silica plates 60 F254, purchased from Merck. All the synthesized products were purified by using column chromatography on 100-200 mesh silica. Melting points were determined on Stuart SMP30 apparatus using an open capillary method with ramp rate of 5 °C min^{-1} and are uncorrected.

NMR spectra were recorded on a JEOL-USA (JNM-ECX500) spectrometer in $CDCl_3$-d_1 and DMSO-d_6 taking TMS (Tetramethyl Silane) as the internal standard (δ = 0). All ^{1}H NMR spectra in $CDCl_3$ or DMSO-d_6 were recorded at 500 MHz frequency, and all ^{13}C-NMR spectra were recorded at 125 MHz frequency. The coupling constants (J) are reported in Hz and signal multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), quintet (qu), doublet of doublets (dd), multiplet (m), or broad (br. s). FT-IR spectra were acquired on a PerkinElmer Spectrum 2 spectrometer. High-resolution mass spectra were recorded on an advance Bruker Daltonics (impact HD) UHR-QqTOF (ultra-high resolution Qq time-of-flight) mass spectrometer.

The synthesis of *N*-amino -7-azaindole **(b)** was prepared according to the literature report.[10]

Representative Procedures for the preparation of substrates.

EDC.HCl (1.2 mmol) and N, N- Diisopropylethylamine (2.5 mmol) were added to a solution of aromatic carboxylic acid (a) (1.0 mmol), N-amino-7-azaindole (b) (1.0 mmol) and HOBt (1.2 mmol) in dimethylformamide (3.0 mL) and stirred for 12h at room temperature. After the completion, the reaction was diluted with EtOAc (2x30 mL) and then washed with water (5.0 mL), brine solution (5 mL) and dried over Na_2SO_4 filtered and concentrated in vacuum. The resulting residue was purified by column chromatography to give the pure benzamides.

*N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**1a**).* Yield: (213 mg, 90%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (193–195) °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.33 (s, 1H), 8.28 (d, *J* = 4.1 Hz, 1H), 7.93 (dd, *J* = 1.4, 7.5 Hz, 1H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 6.8 Hz, 1H), 7.32 (d, *J* = 3.4 Hz, 1H), 7.27-7.24 (m, 2H), 7.11 (dd, *J* = 4.8, 7.6 Hz, 1H), 6.51 (d, *J* = 3.4 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 166.8, 146.2, 141.9, 132.0, 130.6, 130.4, 130.2, 128.3, 127.6, 119.9, 116.7, 99.3. IR(ATR) cm^{-1}: 3251, 3119, 2940, 1695, 1674, 1580, 1438, 1363, 1267, 1127, 892, 798, 715, 687. HRMS (ESI): calculated for $C_{14}H_{12}N_3O$ $[M + H]^+$: 238.0980, found 238.0977. It was crystallized from dichloromethane.

*4-bromo-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4a**).* Yield: (289 mg, 92%) ; white solid, R_f = 0.4 (Hex/EA = 2/1), mp: (164 –166) °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.93 (s, 1H), 8.25 (d, *J* = 4.8 Hz, 1H), 8.04 (d, *J* = 7.5 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 3.4 Hz 1H), 7.17 (dd, *J* = 4.8 & 7.5 Hz, 1H), 6.57 (d, *J* = 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 165.5, 146.3, 143.2, 131.9, 130.8, 130.4, 129.8, 129.1, 126.4, 118.6, 116.8, 98.7. IR (ATR) cm^{-1}: 3494, 3436, 3180, 2918, 2849, 1668, 1591, 1561, 1484, 1272, 1140, 1069, 1008, 903, 845, 793, 715. HRMS (ESI): calculated for $C_{14}H_{11}BrN_3O$ $[M + H]^+$: 316.0085, found 316.0080.

*4-cyano-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4b**).* Yield: (233 mg, 89%) ; white solid, R_f = 0.45 (Hex/EA = 3/2), mp: (225 – 227) °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.49 (s, 1H), 8.27 (dd, *J* = 1.3, 4.8 Hz, 1H), 8.04 (d, *J* = 8.9 Hz, 2H), 7.99 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 4.1 Hz, 1H), 7.17 (dd, *J* = 5.5, 8.2 Hz, 1H), 6.57 (d, *J* = 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 164.8, 146.0, 141.9, 134.2, 132.2, 130.9, 130.1, 128.2, 120.3, 117.6, 117.1, 115.6, 100.0. IR(ATR) cm^{-1}: 3138, 2955, 2919, 2850, 2225, 1687, 1548, 1365, 1224, 1047, 896, 795, 611, 503. HRMS (ESI): calculated for $C_{15}H_{11}N_4O$ $[M + H]^+$: 263.0933, found 263.0922.

*4-fluoro-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4c**).* Yield: (221 mg, 87%) ; white solid, Rf = 0.4 (Hex/EA = 2/1), mp: (182 – 184) °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.87 (s, 1H), 8.25 (dd, *J* = 1.3, 4.8 Hz, 1H), 8.11 – 8.08 (m, 2H),

8.04 (dd, J = 1.3, 7.5 Hz, 1H), 7.62 (d, J = 3.4 Hz, 1H), 7.45 -7.41 (m, 2H), 7.17 (dd, J = 4.8, 8.2 Hz 1H), 6.57 (d, J = 4.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 165.2, 164.5 (d, $J_{C,F}$ = 250 Hz, C), 146.3, 143.2, 130.6, 130.5 (d, $J_{C,F}$ = 3.5 Hz, C), 129.0, 128.2, 118.5, 116.8, 115.8 (d, $J_{C,F}$ = 21.4 Hz, C), 98.5. IR(ATR) cm^{-1}: 3141, 3072, 2919, 1686, 1599, 1541, 1498, 1363, 1267, 1161, 850, 714, 588. HRMS(ESI) : calculated for $C_{14}H_{11}FN_3O$ $[M + H]^+$: 256.0886, found 256.0860.

*4-iodo-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4d**).* Yield: (329 mg, 91%) ; white solid, R_f = 0.45 (Hex/EA = 2/1), mp: (194–196) ˚C. ^1H NMR (500 MHz, $CDCl_3$) δ 12.86 (s, 1H), 8.26 (dd, J = 1.3, 4.8 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.63-7.56 (m, 4H), 7.31 (d, J = 4.1 Hz, 1H), 7.13 (dd, J = 4.8, 8.2 Hz 1H), 6.52 (d, J = 4.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.2, 146.1, 141.8, 137.6, 130.6, 130.3, 129.9, 129.0, 120.1, 116.9, 99.9, 99.6. IR(ATR) cm^{-1}: 3490, 3430, 3185, 2919, 1668, 1582, 1565, 1481, 1362, 1272, 1004, 901, 761, 611, 500. HRMS (ESI): calculated for $C_{14}H_{10}IN_3ONa$ $[M + Na]^+$: 385.9766, found 385.9760.

*4-nitro-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4e**).* Yield: (267 mg, 95%) ; yellow solid, R_f = 0.3 (Hex/EA = 2/3), mp: (258 – 260) ˚C. ^1H NMR (500 MHz, $CDCl_3$) δ 12.10 (s, 1H), 8.44 (d, J = 8.9 Hz, 2H), 8.27 – 8.24 (m, 3H), 8.05 (dd, J = 1.4, 6.2 Hz, 1H), 7.66 (d, J = 3.4 Hz, 1H), 7.19 (dd, J = 4.5, 7.6 Hz, 1H), 6.60 (d, J = 3.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 164.8, 149.7, 146.1, 143.3, 137.2, 130.2, 129.3, 129.1, 123.9, 118.5, 116.8, 98.8. IR(ATR) cm^{-1}: 3121, 3048, 2921, 1688, 1602, 1591, 1344, 1268, 1131, 1046, 852, 712, 605, 504. HRMS (ESI) : calculated for $C_{14}H_{10}N_4O_3Na$ $[M + Na]^+$: 305.0651, found 305.0645.

*4-chloro-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4f**).* Yield: (230 mg, 85%) ; white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (168 – 170) ˚C. ^1H NMR (500 MHz, DMSO-d_6): δ 11.94 (s, 1H), 8.25 (d, J = 1.3, 4.8 Hz, 1H), 8.05 -8.03 (m, 3H), 7.68 (d, J = 8.2 Hz, 1H), 7.63 (d, J = 3.4 Hz, 1H), 7.17 (d, J = 4.1, 7.5 Hz, 1H), 6.58 (d, J = 3.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 165.3, 146.2, 143.2, 137.3, 130.4, 129.6, 129.1, 128.9, 118.5, 116.7, 98.6. IR(ATR) cm^{-1}: 3126, 2927, 1670, 1594, 1562, 1486, 1362, 1273, 1088, 903, 848, 763, 718, 559, 506. HRMS (ESI) : calculated for $C_{14}H_{11}ClN_3O$ $[M + H]^+$: 272.0591, found 272.0584.

*4-(tert-butyl)-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4g**).* Yield: (260 mg, 89%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (183 – 185) ˚C. ^1H NMR (500 MHz, $CDCl_3$) δ 12.3 (s, 1H), 8.28 (dd, J = 1.3, 4.8 Hz, 1H), 7.93 (dd, J = 1.4, 7.5 Hz, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 3.4 Hz, 1H), 7.22 (d, J = 8.2 Hz 2H), 7.11 (dd, J = 4.8, 8.2 Hz,

1H), 6.51 (d, *J* = 4.1 Hz, 1H), 1.28 (s, 9H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.9, 155.4, 146.4, 142.1, 130.6, 130.3, 127.8, 127.5, 125.3, 120.0, 116.9, 99.4, 34.9, 31.1. IR(ATR) cm^{-1}: 3188, 2957, 2899, 1661, 1608, 1536, 1495, 1359, 1276, 1133, 1014, 916, 853, 791, 762, 609. HRMS (ESI) : calculated for $C_{18}H_{19}N_3ONa$ $[M + Na]^+$: 316.1426, found 316.1421**.**

*3,4-dimethoxy-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4h**).* Yield: (237 mg, 80%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/3), mp: (173 – 175) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 11.67 (s, 1H), 8.24 (dd, *J* = 1.4, 4.8 Hz, 1H), 8.03 (dd, *J* = 1.4, 7.5 Hz, 1H), 7.66 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.60 – 7.58 (m, 2H), 7.17 (dd, *J* = 4.8, 8.2 Hz, 1H), 7.14 (d, *J* = 8.2 Hz 1H), 6.56 (d, *J* = 4.1 Hz, 1H), 3.86 (s , 3H), 3.84 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.7, 152.1, 148.4, 146.3, 143.1, 130.6, 129.0, 123.7, 121.2, 118.5, 116.6, 111.1, 110.6, 98.4, 55.6, 55.5. IR(ATR) cm^{-1}: 3145, 2959, 2938, 2836, 1681, 1587, 1509, 1438, 1363, 1267, 1175, 1022, 858, 733, 590. HRMS (ESI) : calculated for $C_{16}H_{15}N_3O_3Na$ $[M + Na]^+$: 320.1011, found 320.1005.

*4-methoxy-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4i**).* Yield: (216 mg, 81%) ; white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (160 – 162) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 12.68 (s, 1H), 8.27 (d, *J* = 4.1 Hz, 1H), 7.92 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.89 (m, *J* = 8.9 Hz, 2H), 7.32 (d, *J* = 3.4 Hz, 1H), 7.10 (dd, *J* = 4.8, 8.2 Hz 1H), 6.70 (d, *J* = 8.9 Hz, 2H), 6.49 (d, *J* = 3.4 Hz, 1H), 3.79 (s , 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.5, 162.5, 146.3, 142.0, 130.5, 130.2, 129.5, 128.1, 123.1, 119.9, 116.7, 113.5, 99.2, 55.3. IR(ATR) cm^{-1}: 3238, 2932, 2837, 1672, 1606, 1506, 1365, 1256, 1176, 1019, 896, 761, 503. HRMS(ESI) : calculated for $C_{15}H_{14}N_3O_2$ $[M + H]^+$: 268.1086, found 268.1063.

*4-methyl-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4j**).* Yield: (200 mg, 80%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (188 – 190) ˚C. ^1H NMR (500 MHz, $CDCl_3$) δ 12.48 (s, 1H), 8.27 (d, *J* = 4.1 Hz, 1H), 7.92 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 4.1 Hz, 1H), 7.10 (dd, *J* = 4.8, 8.2 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.49 (d, *J* = 3.4 Hz, 1H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.0, 146.2, 142.5, 142.0, 130.4, 130.2, 128.9, 127.9, 127.6, 119.8, 116.7, 99.2, 21.4. IR(ATR) cm^{-1}: 3267, 3131, 2919, 2850, 1666, 1607, 1532, 1500, 1438, 1276, 1182, 908, 738. HRMS(ESI) : calculated for $C_{15}H_{14}N_3O$ $[M + H]^+$: 252.1137 found 252.1156.

*4-(methylthio)-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4k**).* Yield: (223 mg, 79%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (189 -191) ˚C. ^1H NMR (500 MHz, DMSO-d_6): δ 11.78 (s, 1H), 8.24 (dd, *J* = 1.3, 4.8 Hz, 1H), 8.03 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.95 (d, *J* = 8.2 Hz 2H), 7.61 (d, *J* = 3.4 Hz, 1H), 7.43 (d, *J* = 8.9 Hz 2H), 7.17 (dd, *J* = 4.8, 7.5 Hz, 1H), 6.56 (d, *J* = 3.4 Hz, 1H), 2.56 (s , 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 165.8, 146.3, 144.2, 143.1, 130.6,

129.0, 128.1, 127.5, 125.0, 118.5, 116.6, 98.4, 14.0. IR(ATR) cm^{-1}: 3236, 2959, 2920, 1674, 1591, 1486, 1435, 1400, 1290, 1264, 1192, 1097, 1022, 894, 796, 715, 606. HRMS(ESI) : calculated for $C_{15}H_{13}N_3OSNa$ $[M + Na]^+$: 306.0677, found 306.0670.

*N-(1H-pyrrolo[2,3-b]pyridin-1-yl)-2-naphthamide (**4l**).* Yield: (238 mg, 83%) ; Off-white solid, R_F = 0.35 (Hex/EA = 2/1), mp: (198 – 200) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 12.01 (s, 1H), 8.68 (s, 1H), 8.27 (d, *J* = 3.4 Hz, 1H), 8.12 – 8.05 (m, 4H), 7.70 -764 (m, 3H), 7.20 – 7.17 (m, 1H), 6.60 (d, *J* = 4.1 Hz 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.4, 146.3, 143.2, 134.6, 132.0, 130.6, 129.0, 128.5, 128.4, 128.2, 127.7, 127.1, 124.0, 118.6, 116.7, 98.5. IR(ATR) cm^{-1}: 3521, 3205, 2919, 2849, 1665, 1555, 1511, 1437, 1362, 1281, 1195, 1140, 958, 914, 893, 864, 754, 719, 584, 475. HRMS(ESI): calculated for $C_{18}H_{14}N_3O$ $[M + H]^+$: 288.1137, found 288.1131.

*N-(1H-pyrrolo[2,3-b]pyridin-1-yl)thiophene-3-carboxamide (**4m**).* Yield: (216 mg, 89%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (217 – 219) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 13.00 (s, 1H), 8.27 (dd, *J* = 1.35, 4.8 Hz, 1H), 8.11 (d, *J* = 2.05 Hz, 1H), 7.94 (dd, *J* = 1.4, 7.55 Hz, 1H), 7.49 (d, *J* = 4.8 Hz 1H), 7.33 (d, *J* = 3.4 Hz, 1H), 7.13 – 7.11 (m, 2H), 6.51 (d, *J* = 3.45 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.7, 146.3, 142.0, 134.1, 130.7, 130.6, 130.5, 126.6, 126.1, 120.1, 117.0, 99.5. IR(API, cm-1); 3139, 3107, 2904,2790, 1686, 1584, 1542, 1358, 1259, 1195, 1110, 1035, 946, 893, 862, 802, 776, 720, 595. HRMS(ESI) : calculated for $C_{12}H_{10}N_3OS$ $[M + H]^+$: 244.0545, found 244.0565.

*3-methyl-N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4n**).* Yield: (223 mg, 89%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (200 – 202) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 11.78 (s, 1H), 8.25 (dd, *J* = 1.35, 4.8 Hz, 1H), 8.04 (dd, *J* = 1.35, 8.2 Hz, 1H), 7.85-7.82 (m, 2H), 7.61 (d, *J* = 3.45 Hz, 1H), 7.47 (d, *J* = 6.15 Hz 2H), 7.17 (dd, *J* = 4.8, 7.6 Hz, 1H), 6.57 (d, *J* = 4.1 Hz, 1H), 2.41 (s , 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.4, 146.3, 143.1, 138.0, 133.0, 131.7, 130.5, 129.0, 128.6, 128.2, 124.8, 118.5, 116.6, 98.5, 20.9. IR(ATR) cm^{-1}: 3306, 3131, 2917, 1678, 1581, 1522, 1483, 1363, 1269, 1185, 1042, 922, 892, 799, 716, 687, 599, 505. HRMS(ESI) : calculated for $C_{15}H_{13}N_3ONa$ $[M + Na]^+$: 274.0956, found 274.0950.

*N-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide-2,3,4,5,6-d5 {**[D_5] - 1a**}*

The corresponding Benzoic acid-2,3,4,5,6-d_5 was dissolved in DMF and followed by addition of N-amino-7azindole, EDC.HCl, HOBt and DIPEA respectively. The combined reaction mixture was stirred for 12h at room temperature. After the completion, the reaction was diluted with EtOAc (2*30 mL) and then washed with water (5.0 mL), brine

solution (5 mL) and dried over Na_2SO_4 filtered and concentrated in vacuum. The resulting residue was purified by column chromatography to give the pure benzamide.

Yield: (212 mg, 88%) ; Off-white solid, R_f = 0.35 (Hex/EA = 2/1), mp: (195 – 197) ˚C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.90 (s, 1H), 8.27 (d, *J* = 3.8 Hz, 1H), 7.92 (d, *J* = 6.9 Hz, 1H), 7.31 (d, *J* = 3.4 Hz, 1H), 7.10 (d, *J* = 4.8, 8.2 Hz 1H), 6.49 (d, *J* = 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.8 146.2, 141.9, 130.4, 130.4, 130.3, 119.9, 116.7, 99.3. IR(ATR) cm^{-1}: 3598, 2982, 1678, 1582, 1523, 1441, 1363, 1270, 1046, 893, 849, 800, 773, 736, 717, 688, 599, 537. HRMS(ESI): calculated for $C_{14}H_7D_5N_3O$ $[M + H]^+$: 243.1294, found 243.1289.

General procedure for the ruthenium–catalyzed C(sp²)-H alkynylation/annulation

A 15 mL screw cap vial was equipped with magnetic stir bar and charged with *N*-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (1a, 59.2 mg, 0.25 mmol), diphenyl acetylene (2a, 53 mg, 0.3 mmol), Ru(*p*-cymene)$Cl_2]_2$ (7.6 mg, 0.0125 mmol), $AgSbF_6$ (8.5 mg, 0.025 mmol), $Cu(OAc)_2.H_2O$ (100 mg, 0.5 mmol) and DCE (2.0 mL). The reaction was sealed and kept under a preheated oil bath at 120 °C for 16h. The reaction was monitored with TLC and later reaction tube was cooled to room temperature, the reaction mixture was diluted with 5 mL of dichloromethane and filtered with a plug Celite bed, followed by washing with 20 mL of dichloromethane. The combined residue was concentered under reduced pressure, and the resulting crude was purified by column chromatography to provide the desired product 3a (85%).

*3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3a**).* Yield: (87 mg, 85%) ; pale yellow solid, R_f = 0.55 (Hex/EA = 2/1), mp: (153 – 155) ˚C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, *J* = 7.55 Hz, 1H), 8.32 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.78 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.62 (t, *J* = 8.2 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.29-7.16 (m, 6H), 7.12-.7.04 (m, 4H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 7.6 Hz, 1H), 6.35 (d, *J* = 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.0, 146.7, 144.0, 141.9, 137.6, 135.5, 133.1, 132.2, 131.5, 131.3, 129.8, 129.7, 129.3, 128.6, 128.6, 128.2, 128.0, 127.8, 127.2, 127.1, 126.9, 125.9, 125.3, 119.2, 118.5, 117.0, 100.5. IR(ATR) cm^{-1}: 3055, 2959, 2861, 1677, 1613, 1594, 1441, 1302, 1206, 1103, 1074, 1025, 964, 790, 774, 739, 696, 595. HRMS(ESI): calculated for $C_{28}H_{19}N_3ONa$ $[M + Na]^+$: 436.1426, found 436.1420.

*3,4-bis(4-methoxyphenyl)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3b**).* Yield: (97 mg, 82%) ; Off-white solid, R_f = 0.45 (Hex/EA = 1/1), mp: (110 – 112) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.32 (d, *J* = 8.2 Hz, 1H), 8.19

(d, *J* = 4.1 Hz, 1H), 7.89 (dd, *J* = 4.1, 8.2 Hz, 1H), 7.77 (t, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 4.1 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.32 (dd, *J* = 2.0, 8.9 Hz, 1H), 7.19 – 7.16 (m, 2H), 7.12 (m, 2H), 6.86 - 6.83 (m, 3H), 6.58 (dd, *J* = 2.7, 11 Hz, 1H), 6.41 (d, *J* = 3.4 Hz, 1H), 6.27 (dd, *J* = 2.7, 8.2 Hz, 1H), 3.70 (s, 3H), 3.37 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 160.0, 158.4, 158.0, 146.3, 143.3, 142.3, 137.6, 133.6, 132.3, 132.2, 131.5, 130.4, 129.1, 127.6, 127.5, 127.3, 125.6, 124.5, 124.5, 118.1, 117.9, 117.0, 113.7, 113.6, 113.1, 112.3, 112.0, 99.6, 54.9, 54.7. IR(ATR) cm^{-1}: 2951, 2958,2835, 1674, 1613, 1506, 1478, 1432, 1368, 1284, 1243, 1174, 1106, 1027, 827, 798, 772, 704, 561. HRMS (ESI): calculated for $C_{30}H_{23}N_3O_3Na$ $[M + Na]^+$: 496.1637, found 496.1631.

*3,4-bis(4-fluorophenyl)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3c**).* Yield: (82 mg, 73%) ; Off-white solid, R_F = 0.45 (Hex/EA = 2/1), mp: (97 – 99) ˚C. ^1H NMR (500 MHz, DMSO-d_6) δ 8.38 (dd, *J* = 1.4, 8.2 Hz, 1H), 8.24 (dd, *J* = 1.4, 4.8 Hz, 1H), 8.16 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.93 (d, *J* = 3.4 Hz, 1H), 7.88 – 7.84 (m, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.62 – 7.58 (m, 2H), 7.44 – 7.40 (m, 2H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.24 (dd, *J* = 4.1, 7.5 Hz, 1H), 7.10 – 7. 06 (m, 2H), 6.79 (d, *J* = 4.1 Hz, 1H), 6.54 – 6.51 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 162.3 (d, $J_{C,F}$ = 248 Hz, C), 162.1 (d, $J_{C,F}$ = 244.4 Hz, C), 159.5, 146.1, 143.8, 135.7, 134.1, 133.0, 132.9 (d, $J_{C,F}$ = 9.5 Hz, C), 130.8, 130,0 129.5, 128.7, 128.1, 127.7, 125.8, 125.4, 123.0, 118.4, 117.4, 116.5, 116.2 (d, $J_{C,F}$ = 22.6 Hz, C), 115.6 (d, $J_{C,F}$ = 21.4 Hz, C), 99.9, 96.3, 80.5. IR(ATR) cm^{-1}: 3051, 1674, 1599, 1507, 1478, 1433, 1373, 1277, 1217, 1155, 1092, 993, 838, 796,771, 707, 539. HRMS(ESI): calculated for $C_{28}H_{18}F_2N_3O$ $[M + H]^+$: 450.1418, found 450.1412.

*3,4-bis(4-(tert-butyl)phenyl)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3d**).* Yield: (103 mg, 79%) ; Off-white solid, R_f = 0.55 (Hex/EA = 2/1), mp: (183 – 185) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.51 (dd, *J* = 1.4, 8.2 Hz, 1H), 8.33 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.79 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.62 (t, *J* = 8.2 Hz, 1H), 7.51 (t, *J* = 8.2 Hz, 1H), 7.38 (t, *J* = 8.2 Hz, 1H), 7.23 (dd, *J* = 2.0 7.5 Hz, 1H), 7.16-7.11 (m, 2H), 7.09-7.05 (m, 2H), 7.01 (dd, *J* = 2.1, 8.2 Hz, 1H), 6.97-6.91 (m, 3h), 6.70 (d, *J* = 7.55 Hz, 1H), 6.35 (d, *J* = 3.4 Hz, 1H), 1.23 (s, 9H), 1.03 (s, 9H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.1, 150.7, 149.7, 147.0, 144.0, 142.2, 137.7, 133.0, 132.6, 131.2, 130.9, 129.6, 129.3, 129.2, 128.8, 128.5, 126.9, 126.0, 125.2, 124.9, 124.4, 123.6, 119.4, 118.7, 117.0, 100.5, 34.3, 34.2, 31.1, 30.8. IR(ATR) cm^{-1}: 3133, 2958, 2902, 1680, 1605, 1508, 1479, 1362, 1324, 1306, 1269, 1202, 1150, 1138, 1102, 1021, 965, 887, 832, 782, 772, 613, 57, 504. HRMS(ESI) : calculated for $C_{36}H_{36}N_3O$ $[M + H]^+$: 526.2858, found 526.2852.

*3,4-bis(4-chlorophenyl)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3e**).* Yield: (87 mg, 73%) ; Off-white solid, R_f = 0.45 (Hex/EA = 3/2), mp: (140 – 142) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.35 (d, *J* = 7.5 Hz, 1H), 8.20 (d, *J* = 4.1 Hz, 1H), 7.90 (d, *J* = 6.8 Hz , 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.69 – 7.66 (m, 2H), 7.46 (dd, *J* = 2.0, 8.2 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.19 – 7.11 (m, 4H), 6.97 (dd, *J* = 2.0, 8.2 Hz, 1H), 6.584 (dd, *J* = 2.0, 8.2 Hz, 1H), 6.44 (d, *J* = 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.8, 146.1, 143.4, 141.2, 136.7, 134.0, 133.9, 133.1, 132.9, 132.2, 132.0, 131.0, 130.7, 130.2, 129.2, 128.4, 127.8, 127.8, 126.8, 125.5, 124.7, 118.0, 117.2, 117.0, 99.9. IR(ATR) cm^{-1}: 3080, 2921, 2850, 1672, 1614, 1487, 1431, 1396, 1369, 1303, 1250, 1153, 1088, 1015, 963, 829, 758, 703, 673, 603, 491. HRMS(ESI) : calculated for $C_{28}H_{18}Cl_2N_3O$ [M + H]$^+$: 482.0827, found 482.0821.

*3,4-bis(4-bromophenyl)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3f**).* Yield: (113 mg, 80%) ; Off-white solid, R_F = 0.55 (Hex/EA = 3/2), mp: (120 – 122) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.35 (d, *J* = 7.5 Hz 1H), 8.20 (d, *J* = 3.4 Hz, 1H), 7.90 (dd, *J* = 1.4, 7.6 Hz, 1H), 7.80 (t, *J* = 8.2 Hz, 1H), 7.68 – 7.65 (m, 2H), 7.51 (dd, *J* = 2.05, 4.8 Hz, 2H), 7.40 (dd, *J* = 2.0, 8.2 Hz, 1H), 7.29-7.27 (m, 2H), 7.17-7.10 (m, 3H), 6.98 (dd, *J* = 2.0, 8.2 Hz, 1H), 6.91 (dd, *J* = 1.4, 8.2 Hz 1H), 6.45 (d, *J* = 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.8, 146.1, 143.4, 141.1, 136.6, 134.3, 133.9, 133.4, 133.2, 132.2, 131.3, 131.2, 131.1, 130.2, 130.1, 129.7, 129.2, 127.8, 127.7, 125.4, 124.6, 121.8, 120.9, 118.0, 117.2, 117.0, 99.9. IR(ATR) cm^{-1}: 2955, 2926, 2835, 1678, 1614, 1508, 1480 1287, 1246, 1176, 1029, 828, 772, 704. HRMS calculated for $C_{28}H_{17}Br_2N_3ONa$ (M + Na$^+$): 591.9636, found 591.9617.

*3,4-dimethyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3g**).* Yield: (52 mg, 72%) ; Off-white solid, R_f = 0.6 (Hex/EA = 2/1), mp: (190 – 192) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.22-8.19 (m, 2H), 8.11 (dd, *J* = 1.4, 7.6 Hz, 1H), 7.86 (d, *J* = 3.4 Hz, 1H), 7.77 (d, *J* = 4.1 Hz, 1H), 7.58 -7.55 (m, 1H), 7.23 (dd, *J* = 4.1, 7.6 Hz, 1H), 6.73 (d, *J* = 4.1 Hz, 1H), 2.34 (s , 3H), 1.98 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 160.2, 145.9, 143.8, 137.5, 137.2, 133.6, 130.0, 129.6, 127.6, 124.1, 123.7, 118.5, 117.4, 108.4, 100.1, 14.5, 13.6. IR(ATR) cm^{-1}: 2919, 2850, 1663, 1615, 1481, 1431, 1371, 1330, 1299, 1275, 1159, 997, 795, 769, 727, 691, 518, 486. HRMS calculated for $C_{18}H_{15}N_3ONa$ [M + Na]$^+$: 312.1113, found 312.1107.

*3,4-diethyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3h**).* Yield: (55 mg, 70%) ; Off-white solid, R_f = 0.55 (Hex/EA = 2/1), mp: (158 – 160) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20-8.18 (m, 2H), 8.11 (dd, *J* = 1.4, 7.6 Hz, 1H), 7.91-7.83 (m, 3H), 7.57-7.54 (m, 1H), 7.22 (dd, *J* = 4.1, 7.5 Hz, 1H), 6.73 (d, *J* = 3.4 Hz, 1H), 2.84 (q, *J* = 7.5 Hz, 2H), 2.60-2.56 (m, 1H), 2.31-2.27 (m, 1H) 1.24 (t, *J* = 7.5, 3H), 0.97 (t, *J* = 7.6 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d6): δ

160.2, 146.6, 143.6, 142.5, 136.2, 133.6, 131.0, 129.5, 127.8, 126.5, 124.5, 123.5, 118.6, 117.4, 114.3, 100.3, 21.7, 20.0, 14.8, 13.9. IR(ATR) cm^{-1}: 2976, 2919, 1671, 1609, 1474, 1427, 1366, 1330, 1272, 1220, 1093, 1058, 795,768, 697, 625, 505. HRMS calculated for $C_{20}H_{20}N_3O$ $[M + H]^+$: 318.1606, found 318.1635.

*3,4-dipropyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3i**).* Yield: (53 mg, 62%) ; Off-white solid, R_f = 0.55 (Hex/EA = 2/1), mp: (128 – 130) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.19 (d, J = 6.2, Hz, 2H), 8.12-8.10 (m, 1H), 7.87-7.82 (m, 3H), 7.56-7.54 (m, 1H), 7.22 (dd, *J* = 4.8, 8.2 1H), 6.73 (d, *J* = 3.4 Hz, 1H), 2.78 (q, *J* = 4.8 Hz, 2H), 2.55-2.50 (m, 1H), 2.20-2.15 (m, 1H), 1.62 (q, *J* = 7.6, 2H), 1.45-1.37 (m, 2H) 1.08 (t, *J* = 6.9, 3H), 0.62 (t, *J* = 6.8, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 160.2, 146.5, 143.6, 141.6, 136.4, 133.6, 130.9, 129.5, 127.8, 126.5, 124.5, 123.7, 118.5, 117.3, 113.3, 100.2, 30.4, 29.0, 23.2, 22.5, 14.1, 14.0. IR(ATR) cm^{-1}: 2963, 2930, 2871, 1668, 1614, 1372, 1324, 1276, 1155, 1090, 1020, 888, 771, 739, 703, 592, 549. HRMS calculated for $C_{22}H_{24}N_3O$ $[M + H]^+$: 346.1919, found 346.1916.

*4-methyl-3-phenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3j**).* Yield: (52 mg, 60%) ; Off-white solid, R_f = 0.55 (Hex/EA = 3/2), mp: (150 – 152) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.32 (d, *J* = 7.6 Hz, 1H), 8.17 (d, *J* = 4.8 Hz, 1H), 7.95-7.90 (m, 2H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.68 -7.63 (m, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.10-7.06 (m, 2H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.36 (d, *J* = 3.4 Hz, 1H), 2.05 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 159.9, 146.1, 143.2, 141.1, 136.9, 133.8, 132.4, 130.4, 129.6, 129.0, 128.7, 128.6, 127.7,127.7, 127.4, 127.2, 124.8, 124.2, 118.0, 116.9, 110.0, 99.3, 14.5. IR (neat, cm^{-1}): 2956, 2919, 2850, 1674, 1596, 1481, 1433, 1371, 1326, 1272, 1224, 769, 696, 596, 499. HRMS calculated for $C_{23}H_{18}N_3O$ $[M + H]^+$: 352.1450, found 352.1442.

*4-ethyl-3-phenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3k**).* Yield: (62 mg, 68%) ; Off-white solid, R_f = 0.55 (Hex/EA = 2/1), mp: (158 – 160) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.33 (d, *J* = 7.6 Hz, 1H), 8.18 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.97-7.92 (m, 2H), 7.85 (dd, *J* = 1.4, 7.6 Hz, 1H), 7.68 -7.62 (m, 2H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.10-7.07 (m, 2H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.34 (d, *J* = 3.4 Hz, 1H), 2.45 (q, *J* = 7.3Hz, 2H) 1.06 (t, *J* = 7.2, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 159.8, 146.1, 143.2, 141.2, 135.8, 133.8, 132.1, 130.3, 129.4, 128.9, 128.7, 128.3, 127.7, 127.3, 127.2, 125.3, 124.1, 118.0, 116.9, 115.9, 99.4, 21.1, 14.6. IR (neat, cm^{-1}): 2970, 2924. 2850, 1666, 1616, 1592, 1486, 1368, 1273, 1149, 1029, 793, 768, 700, 590, 503. HRMS calculated for $C_{24}H_{20}N_3O$ $[M + H]^+$: 366.1606, found 366.1601. It was crystallized from dichloromethane.

*6-bromo-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5a**).* Yield: (86 mg, 70%) ; pale yellow solid, R_f = 0.55 (Hex/EA = 3/2), mp: (168 – 170) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.27 (d, *J* = 8.9 Hz, 1H), 8.21 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.87-7.83 (m, 2H), 7.67 (d, *J* = 4.15 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.30-7.27 (m, 3H), 7.25-7.23 (m, 2H), 7.17 (d, *J* = 6.8 Hz, 1H), 7.11 (dd, *J* = 4.8, 7.5 Hz, 1H), 7.02 (t, *J* = 6.8 Hz, 1H), 6.94-6.89 (m, 2H), 6.71 (t, *J* = 6.8 Hz, 1H), 6.39 (d, *J* = 3.4 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 159.5, 146.1, 143.9, 143.3, 138.8, 134.5, 131.7, 131.2, 131.0, 130.5, 130.2, 130.1, 130.0, 129.1, 129.0, 128.4, 128.3, 128.0, 127.6, 127.5, 126.9, 126.6, 123.5, 118.0, 117.1, 116.9, 99.8. IR(ATR) cm^{-1}: 3098, 3026, 2920, 1670, 1590, 1468, 1319, 1278, 1157, 1026, 800, 698. HRMS(ESI): calculated for $C_{28}H_{19}BrN_3O$ [M + H]$^+$: 492.0711, found 492.0704.

*1-oxo-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)-1,2-dihydroisoquinoline-6-carbonitrile (**5b**).* Yield: (75 mg, 69%) ; pale yellow solid, R_f = 0.5 (Hex/EA = 3/2), mp: (253 – 255) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.49 (d, *J* = 8.2 Hz, 1H), 8.21 (d, *J* = 3.4 Hz, 1H), 8.04 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.88 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.68 (d, *J* = 3.4 Hz, 1H), 7.48 (d, *J* = 1.3 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.32-7.24 (m, 4H), 7.18 (d, *J* = 6.9 Hz, 1H), 7.12 (dd, *J* = 4.8, 7.5 Hz 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.95-6.90 (m, 2H), 6.72 (t, *J* = 7.5 Hz, 1H), 6.41 (d, *J* = 3.4 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 159.1, 146.1, 144.3, 143.4, 137.3, 134.1, 131.4, 131.2, 131.1, 130.0, 130.0, 129.9, 129.5, 129.2, 129.1, 128.9, 128.5, 128.4, 127.7, 127.1, 127.0, 126.6, 118.0, 118.0, 117.2, 117.1, 116.0, 100.0. IR(ATR) cm^{-1}: 3055, 2923, 2853, 2223, 1682, 1611, 1561, 1476, 1429, 1369, 1324, 1262, 1185, 1030, 939, 870, 760. HRMS(ESI) : calculated for $C_{29}H_{18}N_4ONa$ [M+Na]$^+$: 461.1378, found 461.1372.

*6-fluoro-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5c**).* Yield: (70 mg, 65%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (185 – 187) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.43 (dd, *J* = 6.2, 8.9 Hz, 1H), 8.21 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.86 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.68 (d, *J* = 3.4 Hz, 1H) 7.55-7.51 (m, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.30-7.22 (m, 4H), 7.17 (d, *J* = 6.2 Hz 1H), 7.10 (dd, *J* = 4.8, 7.5 Hz, 1H), 7.02 (t, *J* = 6.8 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.77 (dd, *J* = 2.7, 10.3 Hz, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.39 (d, *J* = 3.4 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 165.14 (d, $J_{C,F}$ = 250.3 Hz, C), 159.2, 146.2, 143.8, 143.3, 139.8 (d, $J_{C,F}$ = 9.5 Hz, C), 134.7, 131.7, 131.6 (d, $J_{C,F}$ = 38.1 Hz, C), 131.1 (d, $J_{C,F}$ = 15.5 Hz, C), 130.3, 130.0, 129.0 (d, $J_{C,F}$ = 14.3 Hz, C), 128.4, 128.3, 127.5, 126.9, 126.6, 121.5, 118.0, 117.3, 117.1, 116.1, 115.9, 110.6, 110.4, 99.8. IR(ATR) cm^{-1}: 3053, 2921, 2852, 1683, 1618, 1581, 1468, 1432, 1371, 1273, 1213, 1153, 1068, 964, 888, 762, 698. HRMS calculated for $C_{28}H_{19}FN_3O$ [M + H]$^+$: 432.1512, found 432.1507.

*6-iodo-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5d**)*. Yield: (80 mg, 60%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (243 – 245) ˚C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 4.8 Hz, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.84 (dd, *J* = 2.1, 8.9 Hz, 1H), 7.78 (dd, *J* = 1.4, 7.5 Hz, 1H), 7.63 (d, *J* = 1.4 Hz, 1H), 7.29-7.26 (m, 1H), 7.21-7.18 (m, 3H), 7.15-7.13 (m, 1H), 7.09-7.04 (m, 4H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.35 (d, *J* = 4.1 Hz 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.7, 146.6, 144.1, 143.2, 138.9, 136.3, 134.7, 131.8, 131.4, 131.1, 130.0, 129.6, 129.5, 129.4, 128.4, 128.4, 128.2, 128.1, 127.4, 126.9, 124.4, 118.5,118.1, 117.2, 101.7, 100.7. IR(ATR) cm^{-1}: 2956, 2850, 1684, 1620, 1582, 1489, 1467, 1372, 1273, 1206, 1154, 1068, 964, 888, 833, 791. HRMS calculated for $C_{28}H_{19}IN_3O$ [M + H] $^+$: 540.0573, found 540.0566.

*6-nitro-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5e**)*. Yield: (83 mg, 73%) ; yellow solid, R_f = 0.5 (Hex/EA = 3/2), mp: (207 – 209) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.59 ((d, *J* = 8.25 Hz, 1H), 8.38 (dd, *J* = 2.0, 8.9 Hz, 1H), 8.21 (d, *J* = 4.1 Hz, 1H), 7.92 (dd, *J* = 2.1 Hz, 1H), 7.88 (d, *J* = 6.8 Hz, 1H), 7.70 (dd, *J* = 4.1 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.35-7.26 (m, 4H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.12 (dd, *J* = 4.8, 7.5 Hz 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96-6.91 (m, 2H), 6.73 (t, *J* = 7.5 Hz, 1H), 6.42 (d, *J* = 3.4 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 159.0, 150.4, 146.0, 144.6, 143.4, 137.8, 134.2, 131.4, 131.2, 131.1, 130.2, 130.0, 129.9, 129.2, 128.9, 128.5, 128.2, 127.8, 127.0, 126.6, 121.2, 120.5 118.0, 117.7, 117.2, 100.0. IR(ATR) cm^{-1}: 3056, 2921, 2851, 1687, 1593, 1524, 1490, 1348, 1210, 1144, 1070, 1029, 890, 835, 700, 597. HRMS calculated for $C_{28}H_{19}N_4O_3$ [M + H]$^+$: 459.1457, found 459.1449.

*6-chloro-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5f**)*. Yield: (72 mg, 65%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2),mp: (172– 174) ˚C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, *J* = 8.2 Hz, 1H), 8.33 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.78 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.48 (dd, *J* = 2.0, 7.2 Hz, 1H), 7.29-7.24 (m, 2H), 7.21-7.19 (m, 2H), 7.15-7.13 (m, 1H), 7.10-7.05 (m, 4H), 6.96 (t, *J* = 6.8 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 6.8 Hz, 1H), 6.36 (d, *J* = 3.4 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.4, 146.6, 144.0, 143.4, 140.0, 139.0, 134.8, 131.9, 131.4, 131.1, 130.4, 129.6, 129.5,129.5, 128.5, 128.4, 128.3, 128.1, 127.7, 127.4, 127.0, 125.4, 123.7, 118.6, 118.4 117.2, 100.7. IR(ATR) cm^{-1}: 3054, 2922, 2853, 1680, 1595, 1549, 1468, 1318, 1278, 1150, 1087, 968, 705. HRMS calculated for $C_{28}H_{19}ClN_3O$ [M + H]$^+$: 448.1217, found 448.1212.

*6-(tert-butyl)-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5g**)*. Yield: (94 mg, 81%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (240 – 242) ˚C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, *J* = 8.2 Hz 1H), 8.31 (dd, *J* = 1.2, 4.6 Hz, 1H), 7.77 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.59 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.26-7.21 (m, 4H), 7.20-7.18 (m,

2H), 7.11-7.04 (m, 4H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.0 Hz, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.35 (d, *J* = 4.1 Hz, 1H), 1.25 (s, 9H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 160.9, 156.8, 146.8, 144.0, 141.7, 137.4, 135.6, 132.4, 131.5, 131.2, 129.8, 129.7, 129.3, 128.8, 128.3, 128.1, 128.0, 127.7, 127.0, 126.9, 125.2, 123.0, 122.2, 119.5, 118.5, 117.0, 100.4, 35.3, 30.9. IR(ATR) cm^{-1}: 3023, 2957, 2866, 1682, 1605, 1480, 1433, 1368, 1323, 1278, 1156, 1069, 1029, 846, 750, 694, 599. HRMS calculated for $C_{32}H_{27}N_3ONa$ $[M + Na]^+$: 492.2052, found 492.2049.

*6,7-dimethoxy-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5h**).* Yield: (94 mg, 80%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (280 – 282) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, *J* = 3.4 Hz, 1H), 7.90 (s, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.26-7.25 (m, 2H), 7.19-7.17 (m, 3H), 7.12-7.05 (m, 4H) 6.95 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 6.8 Hz, 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 6.63 (s, 1H), 6.35 (d, *J* = 3.4 Hz, 1H), 3.99 (s , 3H), 3.73 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 160.3, 153.8, 149.2, 146.9, 144.0, 140.6, 135.8, 133.1, 132.4, 131.4, 131.1, 129.9, 129.8, 129.3, 128.7, 128.2, 127.9, 127.8, 127.1, 126.9, 119.1, 118.8, 118.5, 117.0, 108.5, 106.4, 100.4, 56.1, 55.8. IR(ATR) cm^{-1}: 3022,2973, 1665, 1600, 1489, 1392, 1272, 1212, 1113, 1072, 998, 876, 772, 716, 696, 570. HRMS calculated for $C_{30}H_{23}N_3O_3Na$ $[M + Na]^+$: 496.1637, found 496.1631.

*6-methoxy-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5i**).* Yield: (90 mg, 82%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (203 – 205) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.9 Hz, 1H), 8.32 (dd, *J* = 1.4, 4.8 Hz, 1H), 7.76 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.25-7.15 (m, 4H), 7.12-7.04 (m, 5H), 6.95 (t, *J* = 6.9 Hz, 1H), 6.89 (t, *J* = 7.5 Hz 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 2.0 Hz, 1H) 6.34 (d, *J* = 4.1 Hz, 1H), 3.73 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 163.5, 160.7, 146.9, 144.1, 142.6, 139.9, 135.7, 132.4, 131.6, 131.3, 130.9, 129.8, 129.7, 129.4, 128.9, 128.3, 128.1, 128.0, 127.2, 127.0, 119.1, 119.0, 118.6, 117.1, 115.6, 108.3, 100.5, 55.4. IR(ATR) cm^{-1}: 3051, 2935, 2835, 1672, 1607, 1482, 1374, 1232, 1176, 1133, 1031, 833, 769, 704, 576. HRMS calculated for $C_{29}H_{21}N_3O_2Na$ $[M + Na]^+$: 466.1531, found 466.1525.

*6-methyl-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5j**).* Yield: (83 mg, 78%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (206-207) ˚C. ^1H NMR (500 MHz, DMSO-d_6): δ 8.25 (d, *J* = 8.2 Hz, 1H), 8.20 (d, *J* = 4.8 Hz, 1H), 7.85 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.67 (d, *J* = 3.4 Hz, 1H), 7.47 (dd, *J* = 1.3, 8.2 Hz 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.27-7.24 (m, 3H), 7.21-7.15 (m, 2H), 7.09 (dd, *J* = 4.8, 8.2 Hz, 1H), 7.0 (t, *J* = 6.8 Hz, 1H), 6.95-6.92 (m, 2H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.69 (t, *J* = 7.5 Hz, 1H), 6.37 (d, *J* = 3.4 Hz, 1H), 2.35 (s , 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 159.8, 146.2, 144.0, 143.3, 142.4, 137.2, 135.3, 132.1, 131.2, 131.1, 130.4, 130.1, 129.1, 129.0, 128.9, 128.2, 128.0, 127.8, 127.2,

126.8, 126.5, 125.1, 122.4, 118.0, 117.8, 117.0, 99.5, 21.7. IR(ATR) cm^{-1}: 2921, 2864, 1676, 1612, 1556, 1479, 1370, 1321, 1279, 1148, 1110, 1055, 1032, 889, 831, 798, 722, 659, 504. HRMS calculated for $C_{29}H_{21}N_3ONa$ $[M + Na]^+$: 450.1582, found 450.1575.

*6-(methylthio)-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5k**).* Yield: (90 mg, 79%) ; pale yellow solid, R_f = 0.5 (Hex/EA = 3/2), mp: (84 – 86) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.2 Hz, 1H), 8.33 (d, *J* = 4.8 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.36 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.22-7.15 (m, 4H), 7.11-7.05 (m, 4H), 7.01 (d, *J* = 1.4 Hz, 1H), 6.96 (t, *J* = 7.6 Hz 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.72 (t, *J* = 7.6 Hz, 1H), 6.35 (d, *J* = 3.4 Hz, 1H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 160.7, 146.6, 146.0, 143.8, 142.6, 137.8, 135.2, 132.1, 131.4, 131.1 129.6, 129.5, 129.4, 128.7, 128.2, 128.0, 127.8, 127.1, 126.8, 124.4, 121.9, 121.0, 118.6, 117.0, 100.4, 14.5. IR(ATR) cm^{-1}: 3053,2920, 2864, 1672, 1591, 1473, 1432, 1370, 1319, 1276, 1205, 1154, 1069, 1032, 922, 772, 754. HRMS(ESI) : calculated for $C_{29}H_{22}N_3OS$ $[M + H]^+$: 460.1484, found 460.1470

*3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzo[g]isoquinolin-1(2H)-one (**5l**).* Yield: (72 mg, 60%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (323 – 325) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 9.13 (s, 1H), 8.34 (d, *J* = 4.1 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.77 (t, *J* = 6.9 Hz, 2H), 7.69 (s, 1H), 7.56-7.51 (m, 2H), 7.30 (d, *J* = 2.7 Hz, 2H), 7.24-7.22 (m, 3H), 7.13-7.11 (m, 3H), 7.06 (dd, *J* = 4.8, 7.6 Hz 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.35 (d, *J* = 4.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.6, 146.8, 143.9, 140.7, 135.9, 135.6, 133.5, 132.3, 131.6, 131.4, 130.2, 129.9, 129.8, 129.3, 128.8, 128.4, 128.2, 128.1, 128.0, 127.9, 127.1, 126.9, 126.8, 126.5, 125.0, 123.5, 119.2, 118.5, 117.0, 100.4. IR(ATR) cm^{-1}: 3053, 2972, 1671, 1622, 1593, 1489, 1441, 1361, 1272, 1204, 1182, 1056, 1032, 967, 887, 793, 721, 696. HRMS calculated for $C_{32}H_{22}N_3O$ $[M + H]^+$: 486.1576, found 486.1576

*6,7-diphenyl-5-(1H-pyrrolo[2,3-b]pyridin-1-yl)thieno[3,2-c]pyridin-4(5H)-one (**5m**).* Yield: (74 mg, 71%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (206 – 208) ˚C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.34 (dd, *J* = 2.0, 4.8 Hz, 1H), 7.79 (dd, *J* = 1.4, 7.5 Hz, 1H), 7.76 d, *J* = 5.5 Hz, 1H) 7.34 (d, *J* = 5.5 Hz, 1H), 7.28-7.20 (m, 5H), 7.14-7.12 (m, 1H), 7.08-7.06 (m, 3H), 7.00-6.94 (m, 2H), 6.76 (t, *J* = 6.85 Hz, 1H), 6.37 (d, *J* = 4.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 157.2, 151.2, 146.8, 144.1, 141.9, 136.0, 131.5, 130.0, 129.8, 129.4, 129.1, 128.7, 128.4, 128.3, 127.7, 126.1, 125.8, 118.5, 117.1, 116.7, 100.6. IR(ATR) cm^{-1}: 3050, 2971, 2855, 1675, 1581, 1561, 1478, 1427, 1366, 1275, 1054, 1032, 1013, 919, 794, 769, 725, 669. HRMS calculated for $C_{26}H_{18}N_3OS$ $[M + H]^+$: 420.1171, found 420.1153

*7-methyl-3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**5n**).* Yield: (75 mg, 71%) ; Off-white solid, R_f = 0.5 (Hex/EA = 3/2), mp: (177 – 179) ˚C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (d, *J* = 4.8 Hz, 1H), 8.16 (s, 1H), 7.86 (dd, *J* = 1.35, 7.5 Hz, 1H), 7.67 (d, *J* = 3.4 Hz, 1H), 7.62 (dd, *J* = 2.0, 8.2 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.29-7.24 (m, 3H), 7.20 (d, *J* = 6.9 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 7.11-7.07 (m, 2H), 7.0 (t, *J* = 7.6 Hz, 1H), 6.92 (t, *J* = 7.6 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.69 (t, *J* = 6.8 Hz, 1H), 6.37 (d, *J* = 3.4 Hz, 1H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 159.8, 146.2, 143.2, 141.3, 137.3, 135.4, 134.9, 134.8, 132.0, 131.2, 131.0, 130.4, 130.2, 129.2, 129.0, 128.1, 128.0, 127.2, 126.8, 126.5, 125.6, 124.6, 118.0, 117.8, 116.9, 99.5, 20.8. IR(ATR) cm^{-1}: 3100, 3052, 2921, 2859, 1669, 1612, 1590, 1494, 1442, 1372, 1324, 1270, 1222, 1136, 1032, 831, 794, 770, 716, 693. HRMS calculated for $C_{29}H_{22}N_3O$ [M + H]$^+$: 428.1763, found 428.1752

Genereal procedure for the directing group removal

To a solution of 3,4-diphenyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)isoquinolin-1(2H)-one (**3a**) (50 mg, 0.12 mmol) in EtOH (3 mL), $N_2H_4.H_2O$ (30 mg , 0.6 mmol) was added and the resulting mixture was stirred at room temperature for 2 h. After the completion of the reaction, the solvent was evaporated under reduced pressure. The resultant residue was subjected to silica gel column chromatography (EtOAc/Hexane – 2:3) to afford 28 mg (80 %) of 3,4-diphenylisoquinolin-1(2H)-one (3aa) as white solid.[10] ^{1}H NMR (500 MHz, DMSO): δ 11.57 (s, 1H), 8.31 (d, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.29-7.13 (m, 11H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.7, 138.5, 138.1, 135.8, 134.5, 132.5, 131.7, 129.8, 128.2, 128.2, 127.7, 127.0, 126.8, 126.2, 125.0, 124.9, 115.4.

*3,4-dimethylisoquinolin-1(2H)-one (**3gg**).* Yield: (16 mg, 79%) ; pale red solid, R_f = 0.5 (Hex/EA = 3/2), mp: 258 – 260 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.48 (s, 1H), 8.44 (d, *J* = 7.5 Hz, 1H), 7.70-7.65 (m, 2H), 7.47-7.44 (m, 1H), 2.40 (s, 3H), 2.26 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 163.4, 138.9, 133.0, 132.5, 127.5, 125.4, 124.6, 122.7, 108.3, 17.6, 12.5. IR(ATR) cm^{-1}: 3161, 2987, 2865, 1633, 1605, 1547, 1475, 1170, 1009, 912, 763, 705, 652. HRMS calculated for $C_{11}H_{11}NONa$ [M + Na]$^+$: 196.0738, found 196.0733.

*6-(methylthio)-3,4-diphenylisoquinolin-1(2H)-one (**5kk**).* Yield: (33 mg, 82%) ; white solid, R_f = 0.5 (Hex/EA = 3/2), mp: 281 – 283 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.50 (s, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 7.39 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.30-7.20 (m, 8H), 7.14 (d, *J* = 6.9 Hz, 2H), 6.85 (d, *J* = 1.3 Hz, 1H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6): δ 161.4, 144.2, 139.4, 138.4, 135.5, 134.4, 131.7, 129.7, 128.2, 127.7, 127.4, 127.1, 123.5, 121.8, 119.9, 114.7, 13.9. IR(ATR) cm^{-1}:

3100, 3052, 2921, 2859, 1669, 1612, 1590, 1494, 1442, 1372, 1324, 1270, 1222, 1136, 1032, 831, 794, 770, 716, 693. HRMS calculated for $C_{22}H_{18}NOS$ $[M + H]^+$: 344.1109, found 344.1107.

Synthesis of the ruthenium complex – 4j'

A mixture of 4-methyl-*N*-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**4j**) (0.050 g, 0.2 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.122g, 0.2 mmol), and NaOAc (0.033g, 0.4 mmol) was taken in MeOH (10 mL) and heated under reflux for 2 h at 80 °C. The reaction was monitored by TLC and solvent was concentrated in vacuo, and the product was purified by column chromatography on silica gel using dichloromethane : methanol as eluent to afford the **ruthenium complex-4j'** in 41 mg (40 %) yield.. The product was recrystallized from dichloromethane–hexane (1:1) mixture. Yield: (41 mg, 40%) ; deep red crystals, R_f = 0.35 DCM/MeOH (2/1), mp: 205 – 207 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 (d, *J* = 3.4 Hz, 1H), 8.16 (d, *J* = 5.5 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.91(d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.08 (dd, *J* = 5.5, 7.5 Hz, 1H), 6.49 (d, *J* = 4.1 Hz, 1H), 5.23 (d, *J* = 6.2 Hz, 1H), 5.07 (d, *J* = 5.5 Hz, 1H), 4.89 (d, *J* = 6.1 Hz, 1H), 3.90 (d, *J* = 5.5 Hz, 1H), 2.45 (s, 3H), 2.45-2.42 (m, 1H), 2.16 (s, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 174.6, 145.5, 142.4, 139.5, 138.0, 131.6, 130.2,129.7, 128.4, 116.6, 115.0, 98.5, 84.5, 82.6, 30.6, 22.6, 21.5, 21.4, 18.8. IR(ATR) cm^{-1}: 3163, 2967, 2880, 1615, 1579, 1495, 1345, 1298, 1179, 1083, 934, 797. HRMS (ESI) calculated for $C_{25}H_{26}N_3ORu$ $[\{M - Cl\}]^+$: 486.1119, found 486.0893.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Mechanistic details, copies of all ^{1}H NMR & ^{13}C NMR spectra for all new compounds and X-ray crystallographic analysis (PDF)

Accession Codes

CCDC 1868212, 1868597 & 1913752 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road,

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Notes

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REFERENCES

(1) (a) He, R.; Huang, Z.-T.; Zheng, Q.; Wang, C. Isoquinoline skeleton synthesis via chelation-assisted C–H activation. *Tetrahedron Lett*. **2014**, *55*, 5705-5713. (b) Li, X.-C.; Du, C.; Zhang, H.; Niu, J.-L.; Song, M.-P. Cp*-Free Cobalt-Catalyzed C–H Activation/Annulations by Traceless N,O-Bidentate Directing Group: Access to Isoquinolines. *Org. Lett*. **2019**, *21*, 2863-2866.

(2) (a) Collins, T. J.; Ryabov, A. D. Targeting of High-Valent IronTAML Activators at Hydrocarbons and Beyond. *Chem. Rev*. **2017**, *117*, 9140–9162. (b) Kalsi, D.; Dutta, S.; Barsu, N.; Rueping, M.; Sundararaju, B. Room-Temperature C–H Bond Functionalization by Merging Cobalt and Photoredox Catalysis. *ACS Catal*. **2018**, *8*, 8115–8120. and the references cited therein.

(3) (a) Krieger, J.-P.; Lesuisse, D.; Ricci, G.; Perrin, M.-A.; Meyer, C.; Cossy, J. Rhodium(III)-Catalyzed C–H Activation/Heterocyclization as a Macrocyclization Strategy. Synthesis of Macrocyclic Pyridones. *Org. Lett*. **2017**, *19*, 2706–2709. (b) Chen, S.; Bergman, R. G.; Ellman, J. A. Facile Rh(III)-Catalyzed Synthesis of Fluorinated Pyridines. *Org. Lett*. **2015**, *17*, 2567–2569. and the references cited therein.

(4) (a) Yuan, H.; Guo, L.; Liu, F.; Miao, Z.; Feng, L.; Gao. H. Copper-Catalyzed Tandem O-Vinylation of Arylhydroxylamines/[3,3]-Rearrangement/Cyclization: Synthesis of Highly Substituted Indoles and Benzoindoles. *ACS Catal*. **2019**, *9*, 3906-3912. (b) Stuart, D. R.; Alsabeh, P.; Kuhn, M.; Fagnou, K. Rhodium (III)-catalyzed arene and alkene C– H bond functionalization leading to indoles and pyrroles. *J. Am. Chem. Soc*. **2010**, *132*, 18326–18339. and the references cited therein.

(5) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. Highly Regioselective Arylation of sp^3 C-H Bonds Catalyzed by Palladium

Acetate. *J. Am. Chem. Soc*. **2005**, *127*, 13154–13155.

(6) (a) Encyclopedia of Reagents for Organic Synthesis, **2015**, 1-17. (b) Reddy, C.; Bisht, N.; Parella, R.; Babu, S. A. 4-Amino-2,1,3-Benzothiadiazole as a Removable Bidentate Directing Group for the Pd(II)-Catalyzed Arylation/Oxygenation of sp 2 /sp 3 β-C–H Bonds of Carboxamides. *J. Org. Chem*. **2016**, *81*, 12143–12168.

(7) (a) Grigorjeva, L.; Daugulis, O. Cobalt-Catalyzed, Aminoquinoline-Directed C(sp^2)-H Bond Alkenylation by Alkynes**.** *Angew. Chem., Int. Ed.* **2014**, *53* (38), 10209–10212 and references cited therein. (b) Tang, S.; Wang, D.; Liu, Y.; Zeng, L.; Lei, A. Cobalt-Catalyzed Electrooxidative C–H/N–H [4 + 2] Annulation with Ethylene or Ethyne. *Nat. Commun*. **2018**, *9*, 798 and the references cited therein.

(8) (a) Berger, M.; Chauhan, R.; Rodrigues, C. A. B. Maulide, N. Bridging C-H Activation: Mild and Versatile Cleavage of the 8-Aminoquinoline Directing Group *Chem. Eur. J.* **2016**, *22*, 16805 –16808. (b) He, G.; Zhang, S.-Y.; Nack, W. A.; Li, Q.; Chen, G. Use of a Readily Removable Auxiliary Group for the Synthesis of Pyrrolidones by the Palladium-Catalyzed Intramolecular Amination of Unactivated γ C(sp^3)–H Bonds. *Angew. Chem., Int. Ed*. **2013**, *52*, 11124–11128.

(9) (a) Hassan, I. S.; Ta, A. N.; Danneman, M. W.; Semakul, N.; Burns, M.; Basch, C. H.; Dippon, V. N.; McNaughton, B. R.; Rovis, T. Asymmetric δ-Lactam Synthesis with a Monomeric Streptavidin Artificial Metalloenzyme. *J. Am. Chem. Soc*. **2019**, *141*, 4815–4819 and references cited therein. (b) Li, M.; Wang, J.-H.; Li, W.; Lin, C.-D.; Zhang, L.-B.; Wen. L.-R. *N*-Phenoxyamides as Multitasking Reagents: Base-Controlled Selective Construction of Benzofurans or Dihydrobenzofuro[2,3-d]oxazoles. *J. Org. Chem*. **2019**, *84*, 8523-8530 and references cited therein. (c) Guimond, N.; Gouliaras, C.; Fagnou, K. Rhodium(III)-Catalyzed Isoquinolone Synthesis: The N–O Bond as a Handle for C–N Bond Formation and Catalyst Turnover. *J. Am. Chem. Soc.* **2010**, *132*, 6908–6909.

(10) (a) Zhu, M.; Zheng, N. Photoinduced Cleavage of N-N Bonds of Aromatic Hydrazines and Hydrazides by Visible Light. *Synthesis (Stuttg)*. **2011**, *14*, 2223–2236. (b) Zhang, Y.; Tang, Q.; Luo, M. Reduction of Hydrazines to Amines with Aqueous Solution of Titanium(III) Trichloride. *Org. Biomol. Chem.* **2011**, *9*, 4977–4982. (c) Ding, H.; Friestad, G. K. Trifluoroacetyl-Activated Nitrogen-Nitrogen Bond Cleavage of Hydrazines by Samarium(II) Iodide. *Org. Lett.* **2004**, *6*, 637–640.

(11) (a) Grigorjeva, L.; Daugulis, O. Cobalt-Catalyzed, Aminoquinoline-Directed (sp^2)–H Bond Alkenylation by Alkynes. *Angew. Chemie Int. Ed*. **2014**, *53*, 10209–10212 and references cited therein. (b) Shiota, H.; Ano, Y.; Aihara, Y.; Fukumoto, Y.; Chatani, N. Nickel-Catalyzed Chelation-Assisted Transformations Involving Ortho CÀH Bond Activation: Regioselective Oxidative Cycloaddition of Aromatic Amides to Alkynes. *J. Am. Chem. Soc* **2011**, *133*, 14952–14955 and references cited therein. (c)

(12) (a) Su, B.; Wei, J.; Wu, W.; Shi, Z. Diversity-Oriented Synthesis through Rh-Catalyzed Selective Transformations of a Novel Multirole Directing Group. *ChemCatChem* **2015**, *7*, 2986–2990. (b) Zhai, S.; Qiu, S.; Chen, X.; Wu, J.; Zhao, H.; Tao, C.; Li, Y.; Cheng, B.; Wang, H.; Zhai, H. 2-(1-Methylhydrazinyl)Pyridine as a Reductively Removable Directing Group in a Cobalt-Catalyzed C(sp^2)–H Bond Alkenylation/Annulation Cascade. *Chem. Commun*. **2018**, *54*, 98–101.

(13) Hynes John; Doubleday, W. W.; Dyckman, A. J.; Godfrey Jollie D.; Grosso, J. A.; Kiau, S.; Leftheris, K. N-Amination of Pyrrole and Indole Heterocycles with Monochloramine (NH_2Cl). *J. Org. Chem*. **2004**, *69*, 1368–1371.

(14) Allu, S.; Swamy, K. C. K. Ruthenium-Catalyzed Synthesis of Isoquinolones with 8-Aminoquinoline as a Bidentate Directing Group in C–H Functionalization. *J. Org. Chem.* **2014**, *79*, 3963–3972.

(15) (a) Reddy, M. C.; Manikandan, R.; Jeganmohan, M. Ruthenium-Catalyzed Aerobic Oxidative Cyclization of Aromatic and Heteroaromatic Nitriles with Alkynes: A New Route to Isoquinolones. *Chem. Commun*. **2013**, *49*, 6060–6062. (b) Padala, K.; Jeganmohan, M. Highly Regio- and Stereoselective Ruthenium(II)-Catalyzed Direct Ortho-Alkenylation of Aromatic and Heteroaromatic Aldehydes with Activated Alkenes under Open Atmosphere. *Org. Lett*. **2012**, *14*, 1134–1137. (c) Ferrer Flegeau, E.; Bruneau, C.; Dixneuf, P. H.; Jutand, A. Autocatalysis for C–H Bond Activation by Ruthenium(II) Complexes in Catalytic Arylation of Functional Arenes. *J. Am. Chem. Soc*. **2011**, *133*, 10161–10170.