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Ruthenium(II) Catalyzed Regioselective *o*-Amidation of Imidazo-heterocycles with Isocyanates

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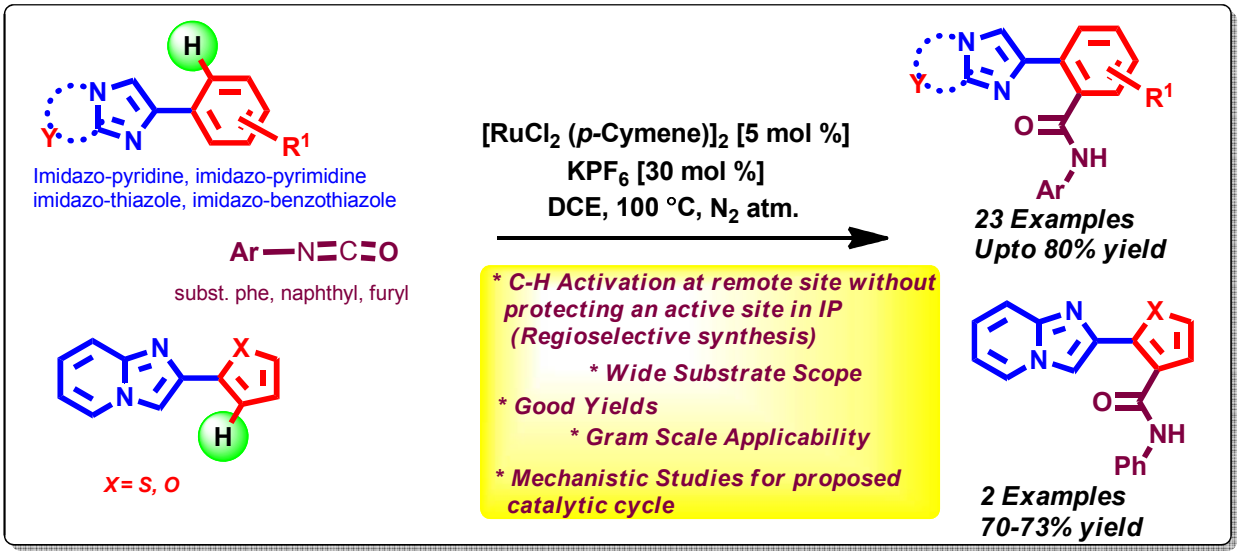


Abstract: Direct *o*-amidation at the phenyl group of 2-phenylimidazo-heterocycles with aryl isocyanates has been achieved *via* chelation-assisted cationic ruthenium(II) complex-catalyzed mechanism. The methodology provides a straightforward, high-yielding regioselective approach towards the synthesis of an array of *o*-amidated phenylimidazo-heterocycles without prior activation of C(sp^2)-H. This also reports the first method for coupling of aryl isocyanates with imidazo[1,2-*a*]pyridine system *via* penta cyclometalated intermediate. The methodology is found to be easily scalable and could be applied towards selective *o*-amidation of 2-heteroarylimidazo[1,2-*a*]pyridine frameworks.

Keywords:

2-Phenylimdazo[1,2-*a*]pyridine ; Aryl isocyanate; Ruthenium catalyst; *o*-Amidation; C-H Activation

Introduction

Transition metal-catalyzed direct C-H activation of non-activated C-H bonds with various coupling partners *via* chelation-assisted activation has streamlined the chemical synthesis by ceasing tedious and expensive substrate pre-activation steps. Within the same domain, immense progress has been recently documented towards the development of pivotal C-C bonds.[1] Chelation-assisted direct C−H bond activation *via* directing group was initially showcased by Pd or Rh catalysts,[2] however, at present the usage of a large variety of other metal catalysts including the environmentally benign Ru catalysts are well exemplified.[3] A multitude of functionalities, including amides, amines, ketones, esters, alcohols and azo group have acted as directing groups in C–H functionalization *via* metal chelation-activation strategy.[4] In 1993, Murai's group utilized a Ru(0)-catalyst precursor for chelation-assisted *o*-alkylation of aromatic ketones with alkenes *via* C–H bond activation.[5] Ever since this work, chelation-assisted Ru(II)-catalyzed addition to C-C π-bonds *via* cyclometalation-migratory insertion mechanism has witnessed enormous progress over Rh or Re catalysis.[6] However, such reactions have not been extended to systems incorporating polar C-N bond, and only proceed in presence of strongly coordinating aryl pyridines or aryl pyrazoles.[7]

Along this line, the direct insertion of activated or non-activated C−H bonds into the polar C−N π-bond of isocyanates is a highly auspicious methodology for providing synthetically and biologically important amides. Pioneering efforts have been made by Ackermann, Kuninobu and Takai, Bergman and Ellman, Cheng and Li towards introducing amide functionalities[7-8] on various biologically important heterocyclic scaffolds, by virtue of versatile directing groups. In most strategies, the directing group (DG) is introduced in the parent moiety to accomplish its *o*-

amidation,[7b,8a-d,8f] while in very few substrate-directed motifs, the *o*-amidation proceeds through an inbuilt coordinating site.[7,8g] (Figure 1).

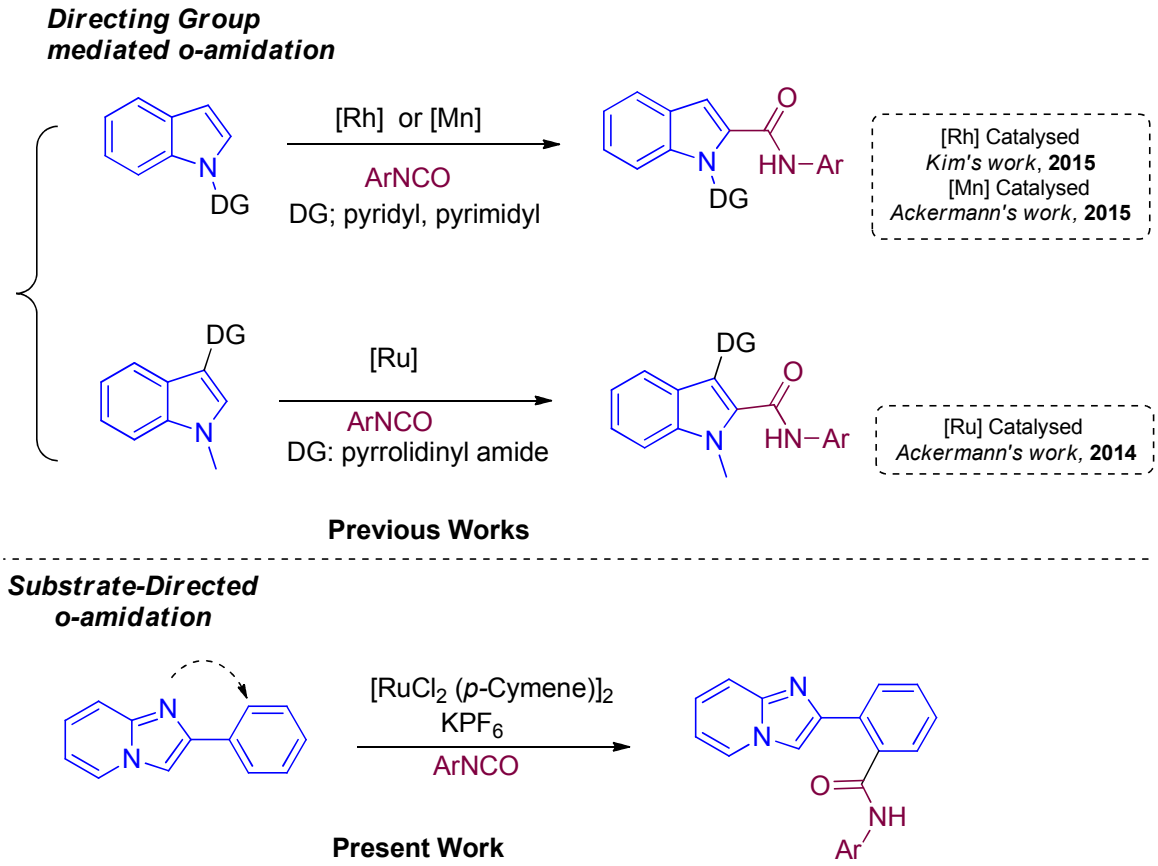


Figure 1. Few examples of Chelation-assisted *o*-amidation of heterocycles (Previous and Present work)

Imidazo[1,2-*a*]pyridine (IP) is an example of privileged heterocyclic motif that has been immensely highlighted in recent literature due to its versatile biological profile including, antiviral, antimicrobial, antitumor, anti-inflammatory, antiparasitic, hypnotic activities.[9] In addition, numerous commercially available drugs such as Alpidem, Zolpidem, Olprinone, minodronic acid, Zolimidine, Nicopidem and optically active GSK812397 candidates are IP functionalized derivatives. In particular, amido functionalized imidazo[1,2-*a*]pyridine scaffold constitute the core skeleton of numerous marketed drugs such as Alpidem, Zolpidem, Saripidem

and others (DS-1, CJ-033466, Q203) that are under clinical trials (Figure 2). [9-10] This allude our interest towards the synthesis of new amido functionalized IPs as potential drug pharmacophores.

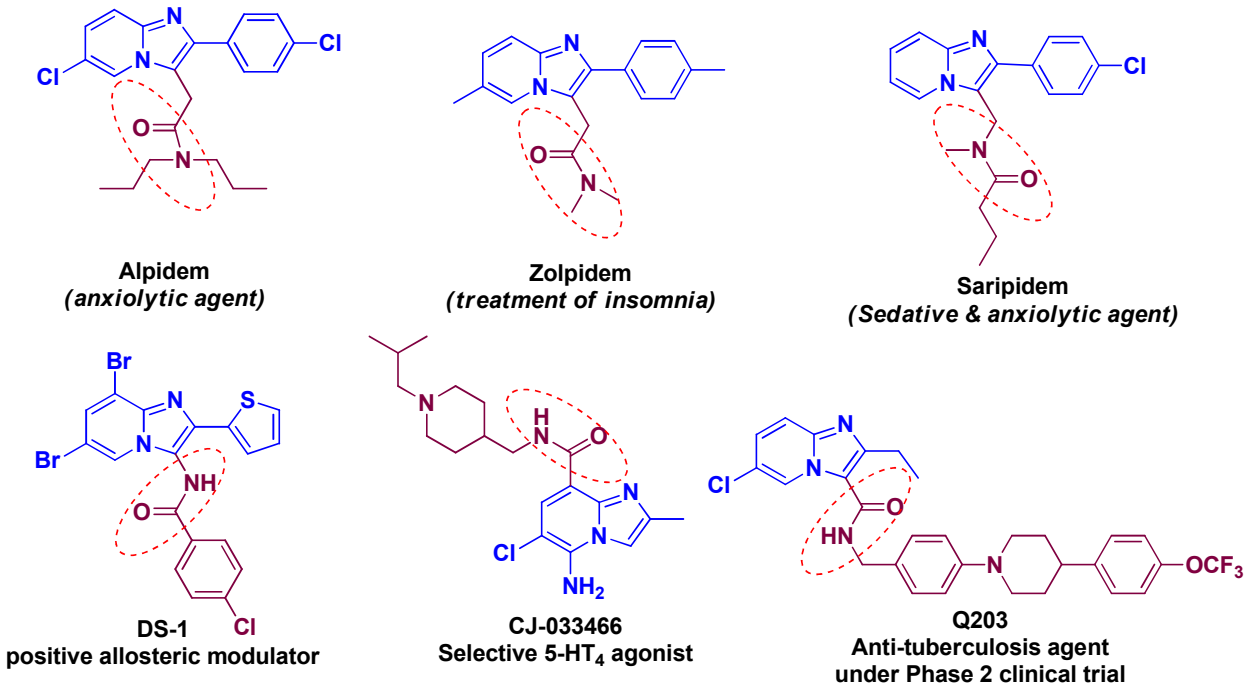


Figure 2. Some examples of biologically active amido functionalized imidazo[1,2-*a*]pyridines

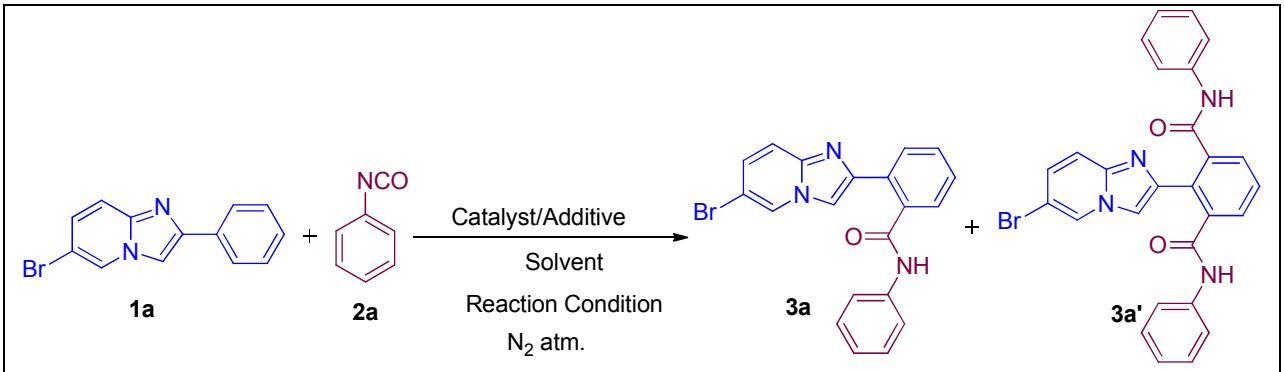
To the best of our knowledge, there is no report for the direct *o*-amidation of 2-arylimidazo[1,2-*a*]pyridines with isocyanate under any metal-catalyzed conditions. Within our program for synthesizing functionalized imidazo[1,2-*a*]pyridines,[11] and hypothesizing it to be self-directing motif, we developed a convergent regioselective Ru(II)-catalyzed approach towards direct *o*-amidation of 2-arylimidazo[1,2-*a*]pyridine with aryl isocyanates.

Results and Discussion

Our initial investigation commenced with the identification of a suitable catalyst and appropriate reaction conditions that would allow selective *o*-amidation on the phenyl ring of 6-bromo-2-phenylimidazo[1,2-*a*]pyridine (**1a**) using phenyl isocyanate (**2a**). To identify an

efficient catalyst for developing the above strategy, we initially employed 5 mol % of [$RuCl_2$ (*p*-cymene)]$_2$ in a variety of solvents such as dichloromethane, toluene, xylene, 1,2-dichloroethane *etc.* under reflux conditions (entry 1). However, the reaction failed to furnish the expected product (**3a**) under any of these conditions, in absence or presence of a variety of additives such as NaOAc, KOAc and CsOAc (Table 1, entry 1-4). Delightfully, the use of $AgSbF_6$ (30 mol%) with [$RuCl_2$ (*p*-cymene)]$_2$ (5 mol%) gave 56% of the expected mono *o*-amidated product (**3a**) along with 25% of *bis o*-amidated product (**3a'**) using DCE at 100 ^oC in 18 h (Table 1, entry 5). Replacing $AgSbF_6$ with $Cu(OAc)_2$ also resulted in similar yields of **3a** and **3a'** (Table 1, entry 6). Interestingly, an employment of comparatively cheaper and stable KPF_6 (30 mol%) resulted in the formation of **3a** and **3a'** in 62% and 20% yields respectively after 18 h (Table 1, entry 7). Gratifyingly, conducting the above reaction for lesser time period (14 h) yielded 72% of **3a** as a major product (Table 1, entry 8). An increment in the catalyst loading from 5 mol % to 10 mol % or additive loading to 50 mol % did not show any noticeable amelioration in the yield of **3a** (Table 1, entry 9-10). On the other hand, reduction in the yield of **3a** was observed when 20 mol % of KPF_6 was used with 5 mol % of the ruthenium catalyst (Table 1, entry 11). Further, an enhancement in the yield of **3a** up to 75% was observed by using 1.5 equivalents of phenyl isocyanate possibly due to the unstable behavior of isocyanate (Table 1, entry 12). Albeit, the change of solvents to toluene, benzene and dichloromethane were less effective for the catalytic reaction giving **3a** in 54, 46 and 48% yields, respectively (Table 1, entries 13-15). The use of other ruthenium catalyst such as $RuCl_2(PPh_3)_3$ and $RuCl_3.xH_2O$ and other available transition metal catalyst including $Rh(OAc)_2$ and $Pd(OAc)_2$ were found to be completely inactive for the above transformation (Table 1, entries 16-19).

Table 1. Selected Optimization[a] of Reaction Conditions for synthesis of **3a**

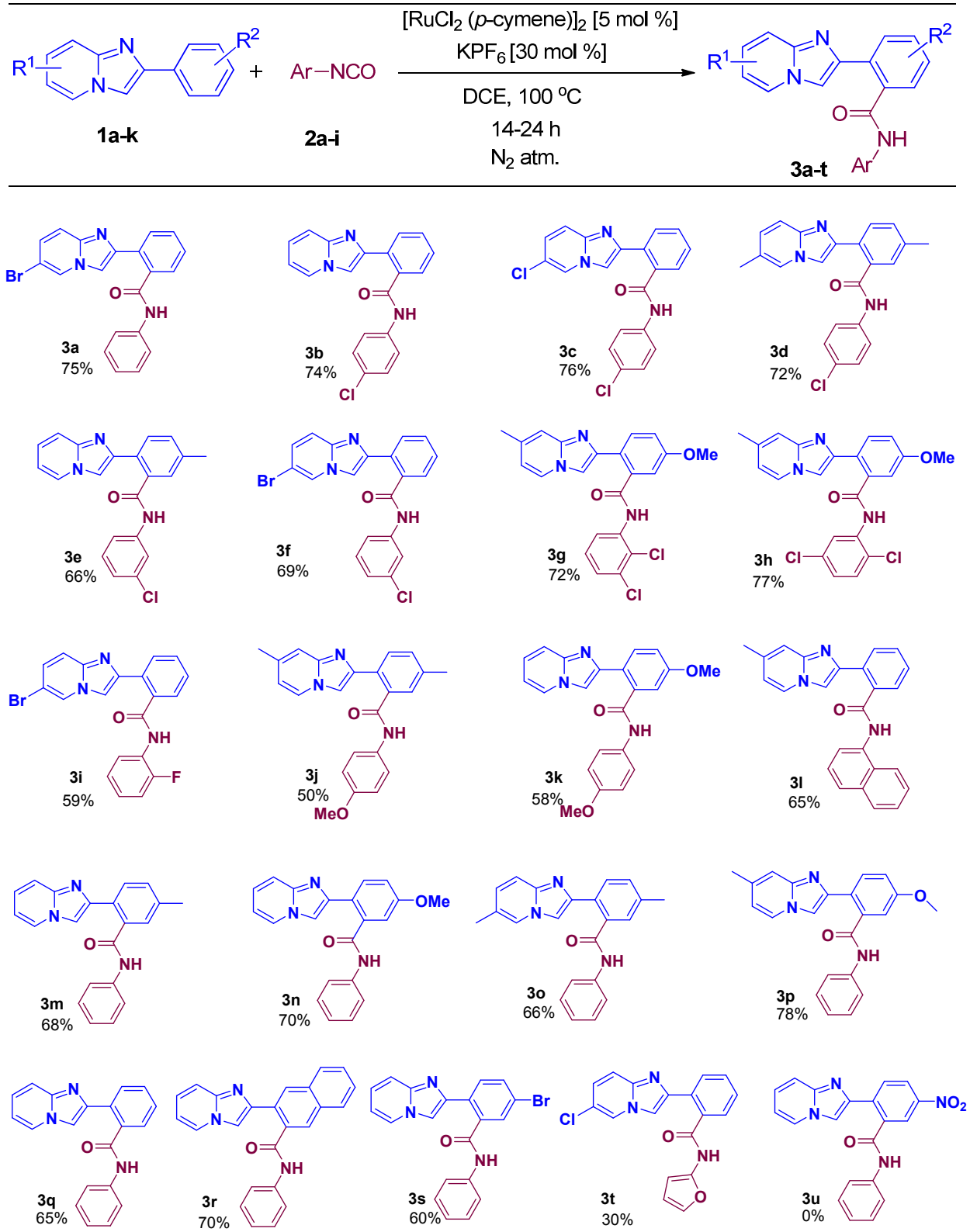


Entry	Catalyst	Additive	Solvent	Yield (%) 3a	Yield (%) 3a'
1	$[RuCl_2\ (p\text{-cymene})]_2$	-	DCE/DCM/xylene/toluene, Reflux, 24 h	NR	-
2	$[RuCl_2\ (p\text{-cymene})]_2$	NaOAc	DCE/ xylene, 100 °C, 24 h	NR	-
3	$[RuCl_2\ (p\text{-cymene})]_2$	KOAc	DCE/ xylene, 100 °C, 24 h	NR	-
4[a]	$[RuCl_2\ (p\text{-cymene})]_2$	CsOAc	DCE/ xylene, 100 °C, 24 h	NR	-
5	$[RuCl_2\ (p\text{-cymene})]_2$	$AgSbF_6$	DCE, 100 °C, 18 h	56	25
6	$[RuCl_2\ (p\text{-cymene})]_2$	$Cu(OAc)_2$	DCE, 100 °C, 18 h	55	22
7	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	DCE, 100 °C, 18 h	62	20
8	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	DCE, 100 °C, 14 h	72	trace
9[b]	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	DCE, 100 °C, 14 h	73	trace
10[c]	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	DCE, 100 °C, 14 h	70	trace
11[d]	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	DCE, 100 °C, 14 h	62	trace
12[e]	**$[RuCl_2\ (p\text{-cymene})]_2$**	**KPF_6**	**DCE, 100 °C, 14 h**	**75**	**trace**
13[e]	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	Toluene, 100 °C, 14 h	54	trace
14[e]	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	Benzene, 80 °C, 14 h	46	trace
15[e]	$[RuCl_2\ (p\text{-cymene})]_2$	KPF_6	DCM, 40 °C, 14 h	48	15
16[e]	$RuCl_2(PPh_3)_3$	KPF_6	DCE, 100 °C, 14 h	NR	-
17[e]	$RuCl_3.\ xH_2O$	KPF_6	DCE, 100 °C, 14 h	NR	-
18[e]	$Rh(OAc)_2$	KPF_6	DCE, 100 °C, 14 h	NR	-
19[e]	$Pd(OAc)_2$	KPF_6	DCE, 100 °C, 14 h	NR	-

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), catalyst (5 mol %), additive (30 mol %), solvent (4 mL). The reactions were performed as per the conditions mentioned; [b]10 mol % of $[RuCl_2\ (p\text{-cymene})]_2$; [c]50 mol % of KPF_6; [d]20 mol % of KPF_6; [e]**2a** (0.37 mmol); NR: No Reaction

With the optimized conditions in hand, the scope of the developed transformation was applied to a variety of aryl isocyanates and a wide range of 2-arylimidazo[1,2-*a*]pyridines (Scheme 1). Among the isocyanates used, chloro substituted phenyl isocyanates (**2b-2e**) showed fairly good

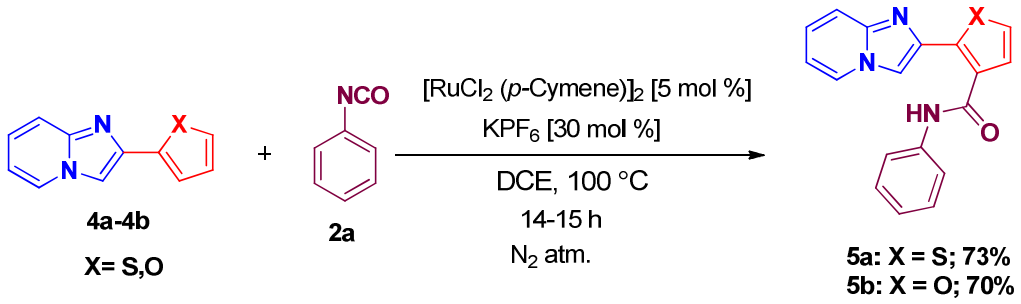
reactivity with the substituted and unsubstituted imidazo[1,2-*a*]pyridines. For example, 4-chlorophenyl isocyanate (**2b**) resulted in the formation of corresponding imidazo[1,2-*a*]pyridin-2-yl benzamides (**3b**, **3c** and **3d**), in 74%, 76% and 72% isolated yields, respectively. While, 3-chlorophenyl isocyanate (**2c**) showed slightly lower reactivity affording **3e** and **3f** in 66% and 69% isolated yields with **1e** and **1a** respectively. The use of 2,5-dichlorophenyl isocyanate (**2d**) gave comparatively better yield of the desired *o*-amidated product (**3h**, 77%) as compared to 2,3-dichlorophenyl isocyanate (**2e**). A reduction in the yield of amidated product (**3i**, 59%) was noticed when 2-fluorophenyl isocyanate (**2f**) was allowed to react with **1a** as compared to phenyl isocyanate (**2a**). 4-Methoxyphenyl isocyanate (**2g**) showed comparative reluctance to react with **1g-h** under the optimized reaction conditions, resulting **3j** and **3k** in 50% and 58% yields respectively. 1-Napthyl isocyanate (**2h**) also reacted well with **1i** to give the corresponding product, **3l** in 65% isolated yield. The presence of an electron donating groups such as methyl and methoxy on the aryl ring of 2-arylimidazo[1,2-*a*]pyridines underwent *o*-amidation affording **3m-p** in fairly good yields. 2-Naphthyl imidazo[1,2-*a*]pyridine (**1j**) also showed similar affinity towards the formation of desired product **3r** in 70% isolated yield. Imidazo[1,2-*a*]pyridine (**1k**) bearing bromo substitution on the aryl ring showcased retardation in its reactivity resulting in 60% of **3s**. Albeit, **3t** was isolated in poor yield when 2-furyl isocyanate (synthesized *in-situ*) was used under similar conditions. Unfortunately nitro substituted imidazo[1,2-*a*]pyridine (**1l**) failed to yield the desired amidated product (**3u**) under our optimized conditions.



Scheme 1. Substrate scope of imidazo[1,2-*a*]pyridines and isocyanates

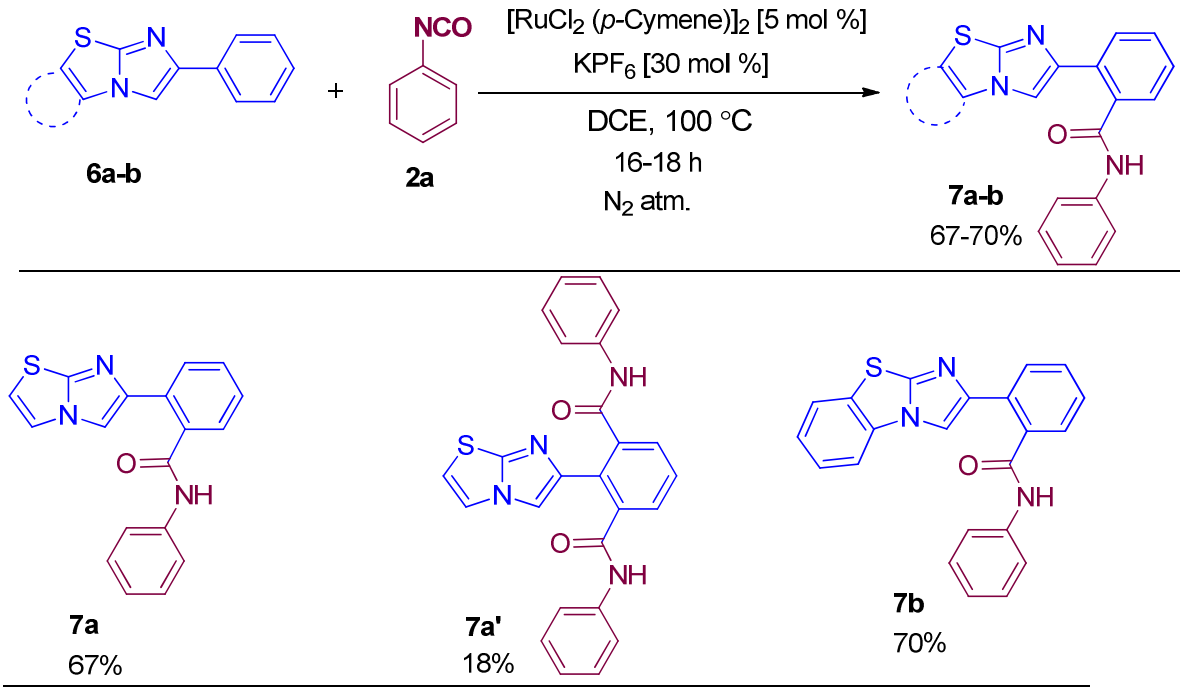
All the synthesized compounds were isolated by column chromatography and characterized by detailed spectroscopic analysis. The ^{1}H NMR spectrum of **3a** showed three characteristic singlets, for one proton each at δ 10.28, 8.39 and 7.92 for the amidic (*N-H*), C-5 *H* and C-3 *H* respectively with other expected signals evidencing the presence of an amidic group at the 2-phenyl ring suggesting the correct structure of the desired compound **3a**. As a representative example, single crystals of **3d** were grown by ethyl acetate/hexanes for the X-ray diffraction studies.[12] **3d** crystallizes in the Monoclinic $P2_1/c$ space group. An ORTEP diagram of **3d** (CCDC No. 1501223) is shown in Figure 2S (Supporting information file).

The scope of the reaction was further explored towards the selective *o*-amidaton of 2-thiophenylimidazo[1,2-*a*]pyridine (**4a**) and 2-furylimidazo[1,2-*a*]pyridine (**4b**) to afford the corresponding *o*-amidated products **5a** and **5b** in 73% and 70% yields, respectively (Scheme 2).



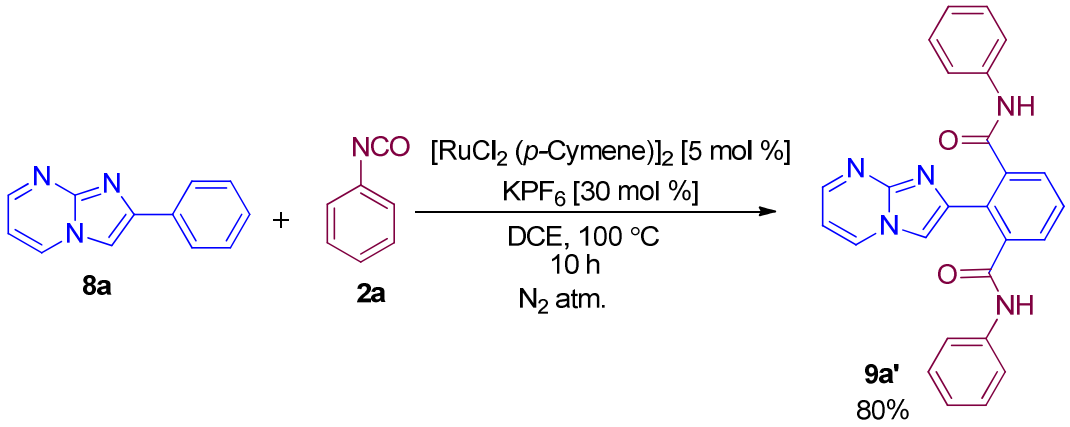
Scheme 2. *o*-Amidation of 2-heteroaryl imidazo[1,2-*a*]pyridines with isocyanate

To extend the scope of our methodology, few other imidazoheterocyles such as imidazo[2,1-*b*]thiazole (**6a**), and benzo[*d*]imidazo[2,1-*b*]thiazole (**6b**) were reacted with phenyl isocyanate (**2a**) under optimized experimental conditions to give their corresponding amidated products **7a** and **7b** in 67% and 70% yields, respectively (Scheme 3). In addition, it was observed that imidazo[2,1-*b*]thiazole (**6a**) showed excellent reactivity and heating for 14 h resulted in the isolation of *bis o*-amidated product (**7a'**) in 18% yield along with **7a**.



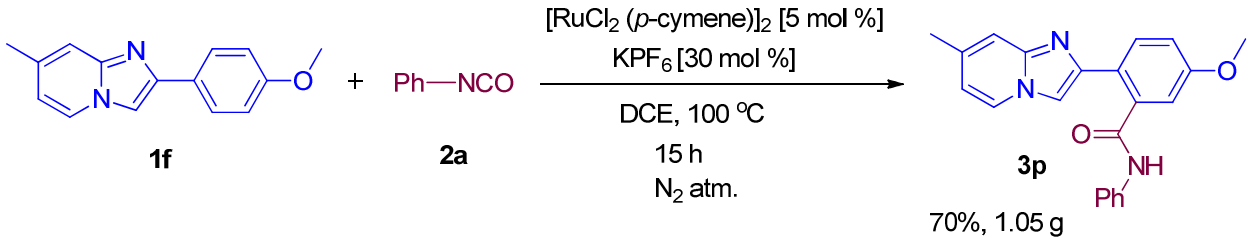
Scheme 3. *o*-Amidation of 2-phenylimidazolyl thiazoles with isocyanate

It is noteworthy that attempts to undergo *o*-amidation of 2-arylimidazo[1,2-*a*]pyrimidine (**8a**) with phenyl isocyanate under similar experimental conditions resulted in predominant formation of *bis o*-amidated product **9a'** in 80% yield even in 10 h. This could possibly be due to presence of an extra nitrogen in the chelating vicinity that enhances its reactivity and restrains the reaction to stop after mono *o*-amidation (Scheme 4).



Scheme 4. *o*-Amidation of 2-phenylimidazo[1,2-*a*]pyrimidine with isocyanate

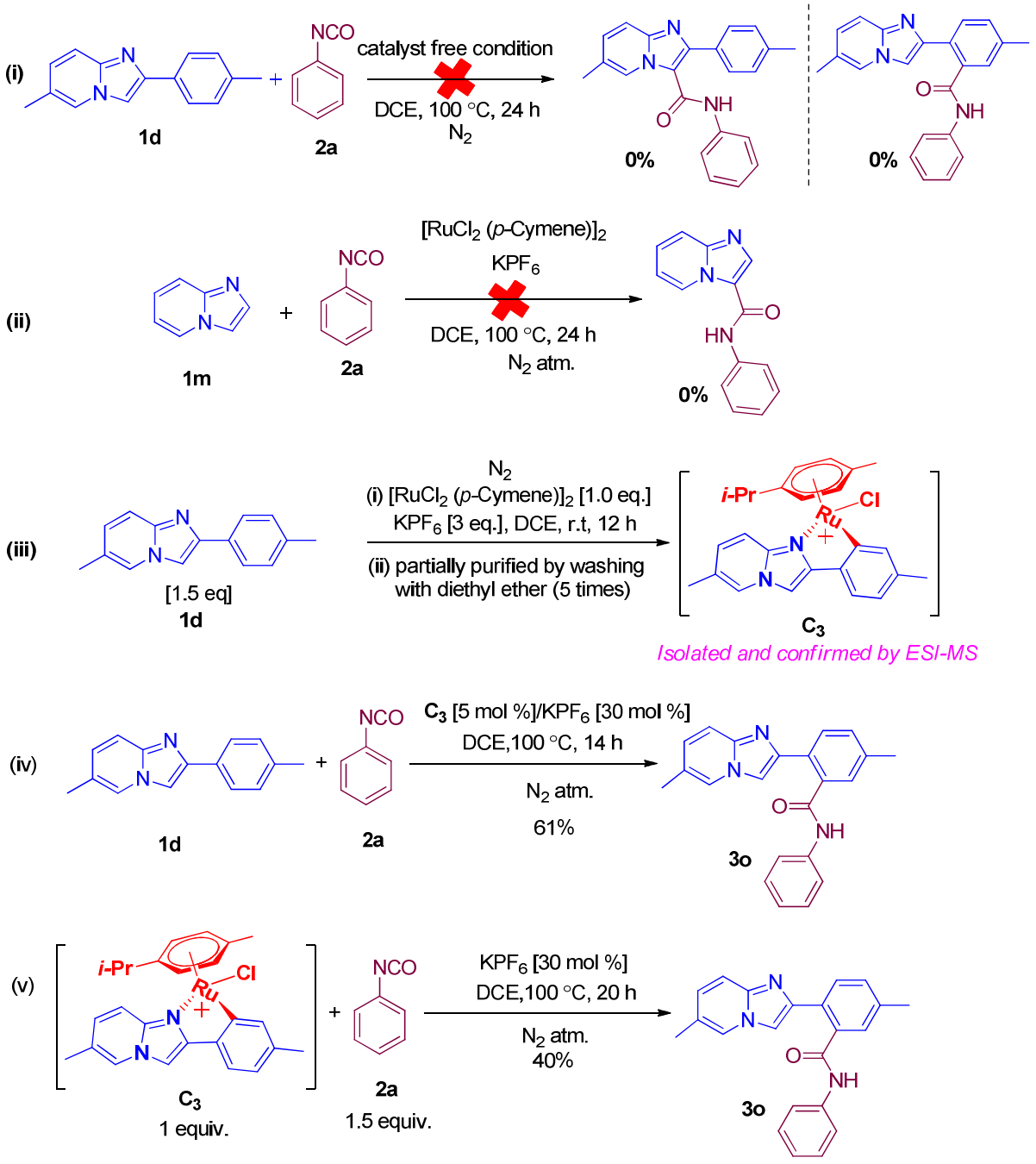
To assess the scalability of this Ru(II)-catalyzed C−H bond amidation process, a gram scale reaction was performed between **1f** and **2a** under optimized conditions to yield the desired *o*-amidated product **3p** in 70% (1.05g) yield, which was a similar to that obtained on a smaller scale (Scheme 5).



Scheme 5. Gram scale synthesis of **3p**

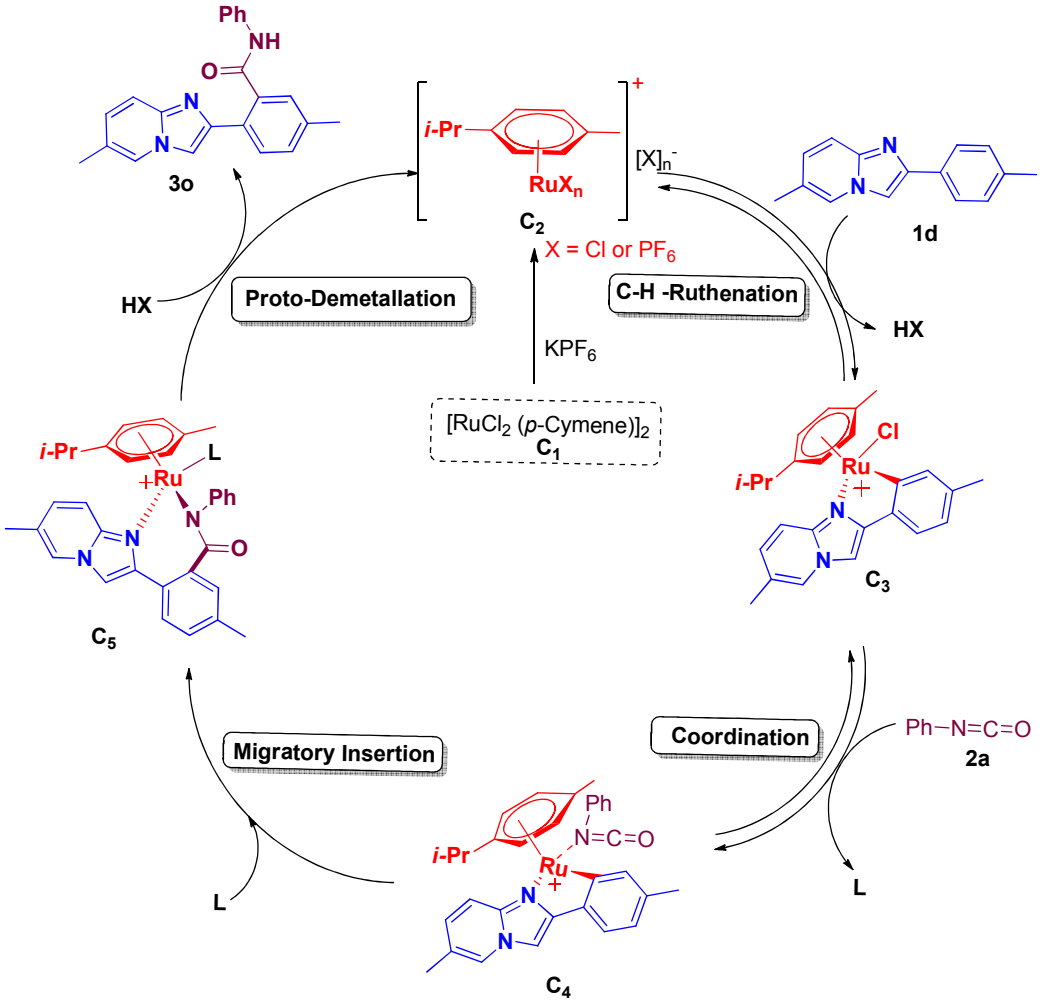
To gain some insights into mechanism, a few control experiments were performed. Stoichiometric reaction between 6-methyl-2-(*p*-tolyl)imidazo[1,2-*a*]pyridine (**1d**) with phenyl isocyanate (**2a**) under catalyst-free conditions failed to yield either C-3 amidated or *o*-amidated product, thereby suggesting a vital role of catalyst and additive (Scheme 6i). The inability of imidazo[1,2-*a*]pyridine (**1m**) to give any amidated product with **2a** under optimized condition further affirmed the non-reactivity of C-3 centre under ruthenium catalyzed conditions (Scheme 6ii). Reaction of **1d** with $[RuCl_2\ (p\text{-cymene})]_2$ in the presence of KPF_6 (3 equiv.) in 1,2-dichloroethane resulted in the formation of cyclometalated complex (**C_3**) (Scheme 6iii). Formation of **C_3** was confirmed by ESI-MS analysis (Fig. 1S, Supporting information file), however, it was only partially purified by repeated diethyl ether wash. Attempts to purify **C_3** by undertaking column chromatography (using silica gel or neutral alumina as adsorbents) were unsuccessful probably due to the instability of the complex. The proposed structure of **C_3** is in accordance with the literature reports.[8a] Employing catalytic amounts of the complex **C_3** for coupling reaction between **1d** and **2a** in the presence of KPF_6 under optimized conditions, the

desired product **3o** was obtained in comparable yields (Scheme 6iv). Finally attempting stoichiometric reaction between $\mathbf{C_3}$ and **1d** also resulted in the formation of **3o** in 40% yield (Scheme 6v), thereby suggesting $\mathbf{C_3}$ to be an intermediate and a reservoir of active species $\mathbf{C_2}$ in the catalytic process.



Scheme 6. Control Experiments

From the control experiments and literature reports[8a,13] it is proposed that the plausible catalytic process is initiated by the dissociation of the $[RuCl_2(p\text{-cymene})]_2$ dimer (**C₁**) into cationic ruthenium monomeric species **C₂** (active catalyst), most likely by substitution of Cl^- ligand by PF_6. Thereafter, reversible C-H ruthenation at the *o*-position of phenyl ring on 2-phenylimidazo[1,2-*a*]pyridine leads to formation of a cationic intermediate complex **C₃**. Coordination of isocyanate **2a** to **C₃**, followed by migratory insertion provides **C₅** *via* **C₄**, which on proto-demetalation affords *o*-amidated product, along with the regeneration of the cationic ruthenium species **C₂** that continues the catalytic process (Scheme 7).



Scheme 7. Plausible catalytic pathway for *o*-amidation of 2-phenylimidazo[1,2-*a*]pyridine with isocyanate

Conclusions

In summary, we have described a convergent and straightforward method for the regioselective synthesis of *o*-amidated imidazo-heterocycles *via* C(sp^2)–H bond functionalization with aryl isocyanates employing $[RuCl_2(p\text{-cymene})]_2$ and KPF_6 in catalytic amounts. An array of *o*-amidated-phenyl imidazo[1,2-*a*]pyridines derivatives with broad functionalities were synthesized in moderate to good yields. The developed protocol was also applicable for the selective *o*-amidation of other imidazo-fused heterocycles such as imidazo[2,1-*b*]thiazole, benzo[*d*]imidazo[2,1-*b*]thiazole and imidazo[1,2-*a*]pyrimidine. This the first report for the direct *o*-amidation on imidazo[1,2-*a*]pyridine scaffold using aryl isocyanates.

Experimental Section

General

Commercially available reagents were used without purification. Commercially available solvents were dried by standard procedures prior to use. Nuclear magnetic resonance spectra were recorded on 400 MHz spectrometer and chemical shifts are reported in δ units, parts per million (ppm), relative to residual chloroform (7.26 ppm) or DMSO (2.5 ppm) in the deuterated solvent. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, dd = doublet of doublet and m = multiplet. Coupling constants *J* were reported in Hz. The ^{13}C NMR spectra were reported in ppm relative to deuterochloroform (77.0 ppm) or [d_6] DMSO (39.5 ppm). Melting points were determined on a capillary point apparatus equipped with a digital thermometer and are uncorrected. High resolution mass spectra were recorded with a TOF analyzer spectrometer by using electrospray mode.

General procedure for *o*-amidation of imidazoheterocycles

A mixture of imidazoheterocycles (**1a-k**, **4a-b**, **6a-b and 8a**) (0.37 mmol), aryl isocyanates (**2a-h**) (0.56 mmol), $[RuCl_2$ (*p*-cymene)$]_2$, (0.02 mmol), KPF_6 (0.11 mmol) in dichloroethane (10 mL) were heated at 100 °C under nitrogen atmosphere for 14- 20 h. On completion of reaction as indicated by TLC, the reaction mixture was filtered, evaporated and was directly subjected to silica gel column chromatography [SiO_2 (100-200 mesh), Hexane/EtOAc, 8:2] to yield the *o*-amidated products (**3a-s**, **5a-b**, **7a-b**). In few cases, the *bis o*-amidated product (**3a'**, **7a'**, **9a'**) were also isolated.

2-(6-Bromoimidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylbenzamide (3a): White solid; yield: 109 mg (75%); mp: 198–201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (s, 1H), 8.39 (s, 1H), 7.99 (d, J = 7.8 Hz, 1H), 7.92 (s, 1H), 7.67 – 7.63 (m, 2H), 7.52 – 7.44 (m, 2H), 7.41 – 7.35 (m, 2H), 7.23 (t, J = 7.9 Hz, 2H), 7.15 (dd, J = 9.5, 1.8 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 148.6, 147.9, 144.3, 141.7, 135.9, 134.4, 134.2, 133.5, 132.9, 132.7, 132.6, 131.9, 128.6, 125.1, 122.6, 116.3, 111.2; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{15}BrN_3O^+$: 392.0398; found 392.0405 $[M+H]^+$.

***N*-(4-Chlorophenyl)-2-(imidazo[1,2-*a*]pyridin-2-yl)benzamide (3b):** White solid; yield: 95 mg (74%); mp 225–227 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 8.56 (dd, J = 6.8, 1.0 Hz, 1H), 8.09 (s, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 8.9 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.54 – 7.50 (m, 2H), 7.48 – 7.45 (m, 1H), 7.39 (d, J = 8.9 Hz, 2H), 7.25– 7.19 (m,1H), 6.88 – 6.84 (m,1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 144.7, 143.0, 138.7, 136.7, 131.7, 129.8, 129.4, 128.9, 128.0, 127.8, 127.4, 125.3, 121.8, 120.2, 117.0, 112.6, 111.0; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{15}ClN_3O^+$: 348.0903; found 348.0910 $[M+H]^+$.

2-(6-Chloroimidazo[1,2-*a*]pyridin-2-yl)-*N*-(4-chlorophenyl)benzamide (3c): White solid; yield: 107 mg (76%); mp 165–166 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.58 (s, 1H), 8.90 (dd, J = 2.0, 0.8 Hz, 1H), 8.11 (s, 1H), 8.03 (d, J = 7.8 Hz, 1H), 7.74 – 7.69 (m, 2H), 7.61 – 7.55 (m, 2H), 7.53 – 7.47 (m, 2H), 7.41 – 7.37 (m, 2H), 7.28 (dd, J = 9.6, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.8, 144.1, 143.1, 136.7, 131.2, 130.1, 129.4, 129.0, 128.3, 128.2, 127.6, 126.4, 125.4, 121.9, 120.3, 119.5, 117.9, 111.7; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{14}Cl_2N_3O^+$: 382.0513; found 382.0521 $[M+H]^+$.

***N*-(4-Chlorophenyl)-5-methyl-2-(6-methylimidazo[1,2-*a*]pyridin-2-yl)benzamide (3d):** White solid; yield: 100 mg (72%); mp 230–232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.72 (s, 1H), 7.88 (s, 1H), 7.67 (s, 1H), 7.65 (d, J = 8.8 Hz, 2H), 7.60 (s, 1H), 7.50 (t, J = 8.3 Hz, 2H), 7.28 – 7.26 (m, 2H), 7.25 – 7.22 (m, 1H), 7.10 (dd, J = 9.2, 1.4 Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 144.2, 143.4, 138.3, 137.6, 135.4, 131.0,130.6, 130.4, 128.9, 128.8, 128.7,128.1, 123.5, 122.7, 121.0, 116.1, 110.9, 21.1, 18.1; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{19}ClN_3O^+$: 376.1216; found 376.1235 $[M+H]^+$.

***N*-(3-Chlorophenyl)-2-(imidazo[1,2-*a*]pyridin-2-yl)-5-methylbenzamide (3e):** White Solid; yield: 88 mg (66%); mp 220– 221 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (s, 1H), 8.56 (d, J = 6.7 Hz, 1H), 8.07 (s, 1H), 7.98 – 7.90 (m, 2H), 7.58 – 7.46 (m, 2H), 7.40 (d, J = 8.0 Hz, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.24 – 7.18 (m, 1H), 7.14 (d, J = 7.86 Hz, 1H), 6.84 (t, J = 6.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.2, 144.6, 143.1, 141.3, 137.5, 136.4, 133.4, 130.8, 130.7, 129.4, 128.9, 128.5, 127.5, 125.4, 123.6, 119.7, 118.6, 116.9, 112.6, 110.7, 21.0 ; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{17}ClN_3O^+$: 362.1060; found 362.1079 $[M+H]^+$.

2-(6-Bromoimidazo[1,2-*a*]pyridin-2-yl)-*N*-(3-chlorophenyl)benzamide (3f): White solid; yield: 108 mg (69%); mp 217–219 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (s, 1H), 8.98

(d, J = 1.0 Hz, 1H), 8.12 (s, 1H), 8.04 (d, J = 7.7 Hz, 1H), 7.93 (s, 1H), 7.65 – 7.56 (m, 1H), 7.56 – 7.45 (m, 4H), 7.35 (dd, J = 9.3, 7.1 Hz, 2H), 7.15 (dd, J = 7.9, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.0, 143.8, 143.2, 141.1, 136.6, 133.5, 131.2 130.8, 130.1, 129.4, 128.4, 128.3, 128.2, 127.6, 123.7, 119.8, 118.7, 118.1, 111.5, 106.4; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{14}BrClN_3O^+$: 426.0008; found 426.0023 $[M+H]^+$.

***N*-(2,3-Dichlorophenyl)-5-methoxy-2-(7-methylimidazo[1,2-*a*]pyridin-2-yl)benzamide (3g):** White solid; yield: 113 mg (72%); mp 238–240 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J = 7.1 Hz, 1H), 8.50 (dd, J = 8.2, 1.5 Hz, 1H), 8.28 (s, 1H), 7.72 – 7.61 (m, 2H), 7.50 (s, 1H), 7.23 (t, J = 8.1 Hz, 1H), 7.17 (dd, J = 8.0, 1.6 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 6.90 (dd, J = 7.2, 1.6 Hz, 1H), 3.90 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) 160.7, 159.5, 149.1, 146.7, 139.4, 137.0, 132.3, 131.4, 128.6, 127.1, 126.1, 126.1, 121.9, 116.9, 115.7, 114.8, 113.9, 55.8, 21.3; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{18}Cl_2N_3O_2^+$: 426.0776 ; found 426.0793 $[M+H]^+$.

***N*-(2,5-Dichlorophenyl)-5-methoxy-2-(7-methylimidazo[1,2-*a*]pyridin-2-yl)benzamide (3h):** White solid; yield: 121 mg (77%); mp 217–218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J = 7.1 Hz, 1H), 8.67 (d, J = 2.4 Hz, 1H), 8.18 (s, 1H), 7.65 (d, J = 8.7 Hz, 2H), 7.50 (s, 1H), 7.16 (d, J = 8.5 Hz, 1H), 7.06 (d, J = 8.7 Hz, 2H), 6.97 (dd, J = 8.5, 2.4 Hz, 1H), 6.94 – 6.86 (m, 1H), 3.89 (s, 3H), 2.51 (s, 3H). ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 159.1, 150.2, 147.4, 139.6, 135.8, 133.3, 131.4, 129.6, 127.6, 125.6, 123.9, 120.8, 120.2, 116.7, 115.9, 114.9, 113.7, 55.5, 21.5; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{18}Cl_2N_3O_2^+$: 426.0776; found 426.0798 $[M+H]^+$.

2-(6-Bromoimidazo[1,2-*a*]pyridin-2-yl)-*N*-(2-fluorophenyl)benzamide (3i): White solid; yield: 89 mg (59%); mp 225–227 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 9.00 (d, J = 1.1 Hz, 1H), 8.17 (s, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.84 (dd, J = 9.0, 6.5 Hz, 1H), 7.59 (d,

J = 7.3 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.48 (t, *J* = 7.0 Hz, 1H), 7.37 (dd, *J* = 9.5, 1.9 Hz, 1H), 7.24 (dd, *J* = 8.0, 5.5 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.0, 156.6, 154.2, 143.9, 143.1, 136.5, 131.3, 130.0, 129.4, 128.4, 128.2, 127.5, 126.8, 126.7, 126.3, 124.7, 118.1, 116.2, 111.7, 106.4; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{14}BrFN_3O^+$: 410.0304; found 410.0327 $[M+H]^+$.

***N*-(4-Methoxyphenyl)-5-methyl-2-(7-methylimidazo[1,2-*a*]pyridin-2-yl)benzamide (3j):** White solid; yield: 68 mg (50%); mp 192–194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.96 (d, *J* = 6.9 Hz, 1H), 7.65 (s, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 9.0 Hz, 2H), 7.36 (s, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 6.87 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 6.9 Hz, 1H), 3.81 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 156.1, 144.9, 144.0, 138.2, 136.5, 135.8, 132.1, 130.8, 130.4, 130.0, 128.1, 125.0, 121.5, 115.4, 115.3, 114.1, 110.5, 55.5, 21.5, 21.1;HRMS (ESI-TOF) (*m/z*) calculated $C_{23}H_{22}N_3O_2^+$: 372.1712; found 372.1730 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyridin-2-yl)-5-methoxy-*N*-(4-methoxyphenyl)benzamide (3k): White solid; yield: 80 mg (58%); mp 198–201 °C; ^{1}H NMR (400 MHz, MeOH-d_4) δ 8.34 (d, *J* = 6.8 Hz, 1H), 7.88 (d, *J* = 10.4 Hz, 2H), 7.53 (d, *J* = 9.2 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.30 (dd, *J* = 6.8, 2.2 Hz, 1H), 7.20 – 7.11 (m, 2H), 6.89 (dd, *J* = 7.1, 2.0 Hz, 2H), 6.86 (dd, *J* = 4.7, 2.2 Hz, 1H), 3.90 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz MeOH-d_4) δ 169.3, 159.5, 156.8, 144.9, 142.6, 137.5, 131.3, 130.8, 126.4, 125.6, 121.9, 121.4, 115.6, 115.2, 113.7, 113.6, 112.7, 110.2, 54.7, 54.4; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{20}N_3O_3^+$: 374.1504; found 374.1523 $[M+H]^+$.

2-(7-Methylimidazo[1,2-*a*]pyridin-2-yl)-*N*-(naphthalen-1-yl)benzamide (3l): White solid; yield: 90 mg (65%); mp 199–203 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 8.43

(d, J = 6.7 Hz, 1H), 8.09 (s, 1H), 8.01 – 7.75 (m, 5H), 7.68 (d, J = 7.1 Hz, 1H), 7.62 – 7.47 (m, 4H), 7.36 (s, 1H), 7.30 (t, J = 7.4 Hz, 1H), 6.73 (d, J = 6.6 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.7, 145.2, 143.3, 137.3, 135.9, 134.1, 132.1, 129.8, 129.6, 129.2, 128.3, 127.9, 127.1, 126.8, 126.8, 126.0, 126.0, 123.7, 123.5, 115.2, 110.7, 21.3; HRMS (ESI-TOF) (*m/z*) calculated $C_{25}H_{20}N_3O^+$: 378.1606; found 378.1614 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyridin-2-yl)-5-methyl-*N*-phenylbenzamide (3m): White solid; yield: 82 mg (68%); mp 188–190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.10 (d, J = 6.8 Hz, 1H), 7.75 (s, 1H), 7.71 (s, 1H), 7.68 – 7.61 (m, 4H), 7.33 (d, J = 7.7 Hz, 3H), 7.26 – 7.21 (m, 1H), 7.10 (t, J = 7.4 Hz, 1H), 6.83 (t, J = 6.8 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 144.6, 138.7, 138.4, 135.8, 131.0, 130.5, 130.0, 129.0, 128.1, 125.9, 125.4, 124.2, 123.2, 120.0, 119.9, 117.0, 112.8, 21.1; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{18}N_3O^+$: 328.1449; found 328.1455 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyridin-2-yl)-5-methoxy-*N*-phenylbenzamide (3n): White solid; yield: 89 mg (70%); mp 179–181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.12 (d, J = 6.6 Hz, 1H), 7.71 (s, 1H), 7.63 (d, J = 7.3 Hz, 3H), 7.46 (d, J = 2.2 Hz, 1H), 7.32 (d, J = 7.9 Hz, 2H), 7.25 (d, J = 8.3 Hz, 1H), 7.22 – 7.16 (m, 1H), 7.11 – 7.03 (m, 2H), 6.85 (t, J = 6.6 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 159.6, 144.4, 138.7, 137.1, 132.3, 128.9, 128.8, 125.9, 125.6, 124.1, 119.8, 119.6, 116.9, 116.8, 114.2, 112.9, 111.0, 55.5; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{18}N_3O_2^+$: 344.1399; found 344.1406 $[M+H]^+$.

5-Methyl-2-(6-methylimidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylbenzamide (3o): White solid; yield: 75 mg (66%); mp 174–176 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.44 (s, 1H), 7.96 (s, 1H), 7.88 (dd, J = 7.9, 2.1 Hz, 1H), 7.79 (dd, J = 8.4, 2.4 Hz, 1H), 7.65 (d, J = 7.1 Hz, 2H), 7.36 (d, J = 9.1 Hz, 1H), 7.30 (s, 1H), 7.28 – 7.17 (m, 3H), 7.04 – 6.93 (m, 2H), 2.36 (s, 3H), 2.21 (s,

3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 143.7, 142.9, 139.4, 137.2, 136.4, 130.3, 129.4, 128.8, 128.6, 128.5, 128.2, 124.0, 123.8, 121.9, 120.1, 116.2, 110.3, 21.1, 18.0; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{20}N_3O^+$: 342.1606; found 342.1612 $[M+H]^+$.

5-Methoxy-2-(7-methylimidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylbenzamide (3p): White solid; yield: 102 mg (78%); mp 189–191 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 8.40 (d, J = 6.9 Hz, 1H), 7.97 (d, J = 8.7 Hz, 1H), 7.89 (s, 1H), 7.70 (d, J = 7.8 Hz, 2H), 7.32 (t, J = 7.8 Hz, 2H), 7.28 (s, 1H), 7.13 (dd, J = 8.7, 2.6 Hz, 1H), 7.10 – 7.01 (m, 2H), 6.66 (d, J = 6.9 Hz, 1H), 3.84 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 163.6, 149.6, 147.5, 144.5, 142.6, 140.4, 135.6, 133.9, 131.3, 129.0, 128.8, 125.1, 120.4, 119.9, 119.7, 117.9, 114.4, 60.7, 26.0; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{20}N_3O_2^+$: 358.1555; found 358.1560 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylbenzamide (3q): White solid; yield: 75 mg (65%); mp 184–186 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 8.58 (d, J = 6.1 Hz, 1H), 8.11 (s, 1H), 8.05 (d, J = 7.5 Hz, 1H), 7.70 (d, J = 7.5 Hz, 2H), 7.53 (m, 4H), 7.33 (t, J = 7.1 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.08 (t, J = 6.8 Hz, 1H), 6.87 (t, J = 5.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.8, 144.5, 142.9, 139.7, 137.0, 131.4, 129.9, 129.4, 129.1, 128.1, 128.0, 127.9, 125.8, 124.0, 120.3, 117.0, 112.8, 111.1; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{16}N_3O^+$: 314.1293; found 314.1303 $[M+H]^+$.

3-(Imidazo[1,2-*a*]pyridin-2-yl)-*N*-phenyl-2-naphthamide (3r): White solid; yield: 94 mg (70%); mp 190–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.12 (d, J = 7.4 Hz, 2H), 8.04 (s, 1H), 7.84 (s, 1H), 7.81 – 7.74 (m, 1H), 7.67 (d, J = 7.6 Hz, 3H), 7.60 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 5.9, 2.8 Hz, 2H), 7.38 – 7.29 (m, 3H), 7.12 (t, J = 7.3 Hz, 1H), 6.87 (t, J = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 206.9, 139.0, 135.7, 133.3, 131.8, 128.76, 128.7, 128.7,

128.2, 127.9, 127.4, 126.9, 126.1, 125.6, 124.2, 123.9, 119.9, 117.6, 116.6, 112.7, 111.2, 111.2; HRMS (ESI-TOF) (*m/z*) calculated $C_{24}H_{18}N_3O^+$: 364.1449; found 364.1454 $[M+H]^+$.

5-Bromo-2-(imidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylbenzamide (3s): White solid; yield: 87 mg (60%); mp 200–203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (s, 1H), 8.08 (d, J = 6.8 Hz, 1H), 7.87 (d, J = 2.0 Hz, 1H), 7.78 (s, 1H), 7.72 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 8.4 Hz, 2H), 7.47 (dd, J = 8.3, 2.1 Hz, 1H), 7.36 (t, J = 7.9 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.14 (t, J = 7.4 Hz, 1H), 6.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 144.6, 142.9, 138.6, 137.4, 132.9, 132.1, 131.6, 129.1, 125.9, 125.9, 124.4, 122.2, 119.9, 117.0, 113.2, 111.3; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{15}BrN_3O^+$: 392.0398; found 392.0403 $[M+H]^+$.

Procedure for the *o*-amidation of 1c with furyl isocyanate (2i)

Furyl isocyanate was synthesized *in-situ* by heating furan-2-carbonyl azide[14] (0.150 g) in 1,2-dichloroethane at 100 °C for about 45 minutes under nitrogen atmosphere *via* curtius rearrangement. Furyl isocyanate (assuming 100% conversion) was directly used for the *o*-amidation of **1c** (0.100 g, 0.43 mmol) following earlier described procedure to yield **3t**.

2-(6-Chloroimidazo[1,2-*a*]pyridin-2-yl)-*N*-(furan-2-yl)benzamide (3t): Yellow solid; yield: 66 mg (30%); mp 200–203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.89 (s, 1H), 7.65 (s, 1H), 7.60 (d, J = 9.5 Hz, 1H), 7.47 – 7.40 (m, 3H), 7.36 (dd, J = 7.3, 5.3 Hz, 2H), 7.27 – 7.24 (m, 1H), 7.23 – 7.19 (m, 1H), 6.69 (dd, J = 3.4, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 146.5, 145.5, 129.8, 128.8, 128.5, 127.3, 125.2, 121.3, 120.3, 120.3, 117.8, 117.2, 112.9; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{13}ClN_3O_2^+$: 338.0696; found 338.0675 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylthiophene-3-carboxamide (5a): White solid; yield: 86 mg (73%); mp 221–223 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.52 (s, 1H), 8.65 – 8.60 (m, 1H), 8.43 (s, 1H), 7.80 (d, J = 7.7 Hz, 2H), 7.68 (dd, J = 9.1, 0.7 Hz, 1H), 7.63 (d, J = 5.3

Hz, 1H), 7.51 (d, *J* = 5.3 Hz, 1H), 7.42 – 7.30 (m, 3H), 7.14 – 7.08 (m, 1H), 6.96 (td, *J* = 6.8, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 144.3, 139.7, 138.3, 137.9, 133.6, 130.6, 129.3, 127.7, 126.7, 125.7, 124.1, 120.3, 116.7, 113.4, 111.9; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}N_3OS^+$: 320.0857; found 320.0885 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyridin-2-yl)-*N*-phenylfuran-3-carboxamide (5b): White solid; yield: 75 mg (67%); mp 180–182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.77 (s, 1H), 8.69 (m, 1H), 8.53 (d, *J* = 0.5 Hz, 1H), 7.94 – 7.86 (m, 4H), 7.50 (m, 1H), 7.46 – 7.40 (m, 2H), 7.16 – 7.09 (m, 2H), 7.05 (d, *J* = 1.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.7, 151.4, 148.9, 147.8, 147.7, 144.9, 140.3, 134.3, 132.6, 128.5, 124.9, 124.4, 121.5, 119.1, 118.9, 117.2; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}N_3O_2^+$: 304.1086; found 304.1092 $[M+H]^+$.

2-(Imidazo[2,1-*b*]thiazol-6-yl)-*N*-phenylbenzamide (7a): Yellow solid; yield: 80 mg (67%); mp 195–198 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 7.96 (t, *J* = 6.7 Hz, 2H), 7.92 (s, 1H), 7.70 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.50 (m, 1H), 7.46 (d, *J* = 6.5 Hz, 1H), 7.40 (t, *J* = 7.0 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 4.4 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.0, 149.2, 144.7, 139.8, 136.2, 131.7, 129.8, 129.1, 128.7, 128.0, 127.4, 124.0, 120.6, 120.2, 113.6, 111.4; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}N_3OS^+$: 320.0857; found 320.0864 $[M+H]^+$.

2-(Benzo[*d*]imidazo[2,1-*b*]thiazol-2-yl)-*N*-phenylbenzamide (7b): White solid; yield: 95 mg (70%); mp 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.92 (s, 1H), 7.80 – 7.72 (m, 2H), 7.66 (dd, *J* = 7.3, 4.7 Hz, 3H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.36 (m, 4H), 7.13 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 147.5, 145.4, 138.5, 135.6, 132.0, 131.0, 130.2, 130.1, 129.8, 129.0, 128.9, 128.9, 128.0, 126.4, 125.2, 124.3, 120.0, 113.0, 110.2; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{16}N_3OS^+$: 370.1014; found 370.1022 $[M+H]^+$.

2-(6-Bromoimidazo[1,2-*a*]pyridin-2-yl)-*N*^{1},*N*^{3}-diphenylisophthalamide (3a') : White solid; yield[(Table 1, entry 5)]: 25%; mp 240–242 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.30 (s, 2H), 8.97 (d, J = 1.1 Hz, 1H), 8.03 (s, 1H), 7.70 – 7.67 (m, 2H), 7.63 – 7.59 (m, 1H), 7.54 (d, J = 7.7 Hz, 4H), 7.39 (d, J = 9.6 Hz, 1H), 7.29 – 7.24 (m, 5H), 7.04 (t, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.7, 142.7, 142.6, 139.5, 139.3, 129.8, 129.0, 128.9, 128.3, 127.9, 127.3, 123.9, 120.3, 118.1, 112.8, 106.3; HRMS (ESI-TOF) (*m/z*) calculated $C_{27}H_{20}BrN_4O_2^+$: 511.0769; found 511.0778 $[M+H]^+$.

2-(Imidazo[2,1-*b*]thiazol-6-yl)-*N*^{1},*N*^{3}-diphenylisophthalamide (7a'): Yellow solid; yield: 0.024 mg (18%); mp 224–225 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.27 (s, 2H), 7.92 (d, J = 4.5 Hz, 1H), 7.83 (d, J = 3.8 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.60 – 7.52 (m, 5H), 7.28 (t, J = 7.9 Hz, 4H), 7.16 (d, J = 4.5 Hz, 1H), 7.05 (t, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.9, 148.5, 142.8, 139.6, 139.0, 130.0, 128.9, 128.7, 127.6, 123.8, 120.3, 120.2, 113.2, 112.6; HRMS (ESI-TOF) (*m/z*) calculated $C_{25}H_{19}N_4O_2S^+$: 439.1228; found 439.1236 $[M+H]^+$.

2-(Imidazo[1,2-*a*]pyrimidin-2-yl)-*N*^{1},*N*^{3}-diphenylisophthalamide (9a'): Yellow solid; yield: 127 mg (80%); mp 273–275 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.40 (s, 2H), 9.04 – 8.98 (m, 1H), 8.42 (d, J = 1.9 Hz, 1H), 8.00 (s, 1H), 7.70 (d, J = 7.4 Hz, 2H), 7.66 – 7.61 (m, 1H), 7.57 (d, J = 7.9 Hz, 4H), 7.27 (t, J = 7.7 Hz, 4H), 7.04 (t, J = 7.3 Hz, 2H), 6.98 (dd, J = 6.5, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.7, 150.5, 147.4, 143.0, 139.6, 139.4, 135.4, 130.0, 129.0, 128.9, 128.4, 124.0, 120.3, 110.7, 109.3; HRMS (ESI-TOF) (*m/z*) calculated $C_{26}H_{20}N_5O_2^+$: 434.1617; found 434.1625 $[M+H]^+$.

Procedure for Synthesis of Complex C$_3$. A mixture of 6-methyl-2-(*p*-tolyl)imidazo[1,2-*a*]pyridine (**1d**) (0.17 mmol, 0.040 g), $[RuCl_2$-(*p*-cymene)$]_2$, (0.11 mmol, 0.070 g), KPF_6 (3 equiv.) in dichloroethane (5 mL) under nitrogen atmosphere was stirred for 12 h. After filtration

through celite, the solvent was concentrated under reduced pressure and the residue was washed with Et_2O (15 mL×5) to afford partially purified complex **C_3**. ESI-MS (*m/z*) calculated $C_{25}H_{27}N_2Ru^+$: 457.1217; found 457.1382 $[M\text{-}Cl]^+$.

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SUPPORTING INFORMATION

Copies of NMR data, ESI-MS of C_3, single crystal X-ray analysis data table for **3d** and ORTEP diagram of **3d**. A CIF file for **3d** which is deposited with Cambridge Crystallographic Data Centre (CCDC No. 1501223) is provided.

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(12) Crystal data for **3d**: $C_{22}H_{18}ClN_3O$, M = 375.84, Monoclinic, space group $P2_1/c$, a = 10.8372(10) Å, b = 10.5719(5) Å, c = 16.5469(8) Å, α = 90°, β = 90.413(1)°, γ = 90°, V = 1895.7(2) $Å^3$, Z = 4, D_c =1.317 Mg/cm^3, μ (Mo-Kα) = 0.218 mm^{-1}, T = 296(2) K, 48825 reflections collected. Refinement of 2619 reflections (246 parameters) with $I>2\sigma(I)$ converged at a final $R_1 = 0.046$, $wR_2 = 0.1098$, gof = 1.057.

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