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Ruthenium-Catalyzed Synthesis of Isoquinolones with 8-Aminoquinoline as a Bidentate Directing Group in C−H Functionalization

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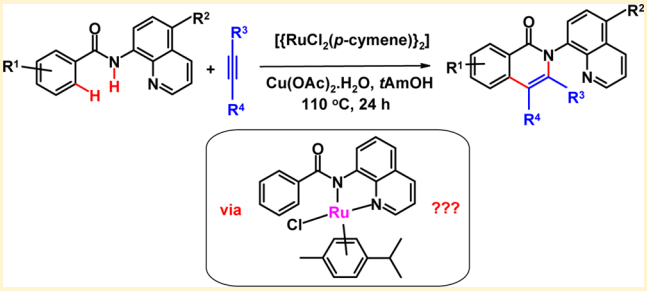
Supporting Information

ABSTRACT: Ruthenium-catalyzed oxidative annulation of *N*-quinolin-8-yl-benzamides with alkynes in open air has been achieved using 8-aminoquinolinyl moiety as a bidentate directing group in the presence of $Cu(OAc)_2·H_2O$ as an oxidant. This reaction offers a broad substrate scope, and both symmetrical and unsymmetrical alkynes can be applied. High regioselectivity was achieved in the case of unsymmetrical (aryl)alkynes. Reaction with heteroaryl amides was also successful in this catalytic process. A ruthenium-*N*-quinolin-8-yl-benzamide complex was isolated in the absence of alkyne; in the absence of both *N*-quinolin-8-yl-benzamide and alkyne, *in contrast to literature*, only the monoacetate complex RuCl(OAc)(*p*-cymene), but not the bis-acetate complex $Ru(OAc)_2$(*p*-cymene), was isolated. These data suggest that this reaction may proceed via *N*,*N*-bidentate chelate complex. Key products were characterized by X-ray crystallography.



INTRODUCTION

Because of the importance of nitrogen-containing heterocycles in biology and materials chemistry, various synthetic routes have been developed for their synthesis and functionalization. These structural motifs are widely present in natural products and medicinally relevant compounds.[1] Transition metal catalyzed C−H functionalization is an important tool in construction of these synthetic targets.[2] After the first report by Murai et al., directing groups received a significant attention, since they selectively activate the proximal C−H bond through metal chelation.[3] A wide variety of structurally simple monodentate directing groups like carbonyl,[4a,b] acid,[4c,d] amide,[4e,f] amine,[4g,h] pyridine,[4i,j] imine,[4k,l] Si,N-type chelation-assisted auxiliary,[4m,n] etc., are well explored in C−H bond transformations. After the discovery of Pd(II)-catalyzed arylation of unactivated sp^3 C−H bonds by Daugulis et al.,[5] the use of bidentate directing groups picolinamide,[6] 8-aminoquinoline,[7] *N*-(2-pyridylsulfonyl),[8] sulfixamine,[9] and 2-methylthioaniline[10] were also explored in C−H bond functionalization, including those in the total synthesis of natural products.

Isoquinolone skeleton is widely found in diverse natural products and medicinally important building blocks; hence, there are many synthetic routes for this class of compounds.[11] Chatani et al. recently reported the [Ru]-catalyzed carbonylation[12a,b] and arylation[12c] of aromatic amides using pyridylmethylamine, and 8-aminoquinoline as bidentate directing groups in which these moieties coordinate in an *N*,*N*-fashion to the ruthenium center. They have also reported the Ni-catalyzed oxidative annulation of aromatic amides with alkynes leading to isoquinolones[13] using pyridylmethylamine as an auxiliary directing group; they find that 8-aminoquinoline as an ineffective directing group for this transformation. In our work here, we have observed that in the presence of $\{[RuCl_2(p\text{-cymene})]\}_2$ and $Cu(OAc)_2$, 8-aminoquinoline directed oxidative annulation takes place. Also, this reaction takes place via the formation of monoacetate complex [RuCl(OAc)(*p*-cymene)] and not the bis-acetate complex $[Ru(OAc)_2(p\text{-cymene})]$, in contrast to the literature reports.[14] Thus, herein we report an efficient and readily applicable method for the synthesis of isoquinolones via oxidative annulation of aromatic amides with alkynes using 8-aminoquinoline as an auxiliary bidentate directing group.

RESULTS AND DISCUSSION

We began our study by investigating the Ru-catalyzed oxidative annulation of *N*-quinolin-8-yl-benzamide **1a** with alkyne **2a**. To this end, we have screened several oxidants and solvents. The reaction of amide **1a** (0.4 mmol) with alkyne **2a** (0.6 mmol) in the presence of $[\{RuCl_2(p\text{-cymene})\}_2]$ (5 mol %)/$Cu(OAc)_2·H_2O$ (0.8 mmol) in *t*AmOH solvent at 110 °C afforded the product **3** in 57% yield (Table 1, entry 1). By increasing the amount of alkyne to 0.8 mmol, complete conversion of the amide occurred, and the product was isolated in excellent yield (74%) (entry 2); the reaction mixture showed complete consumption of the amide. Use of

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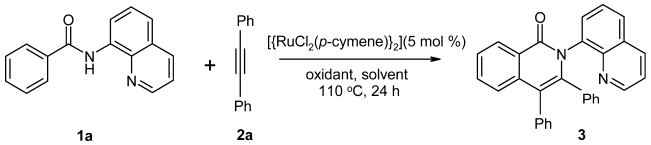
Table 1. Optimization Study for the [Ru]-Catalyzed Oxidative Annulation[a]



1a 2a 3

entry	oxidant	solvent	yield (%)[b]
1	$Cu(OAc)_2·H_2O$	*t*AmOH	57[c]
2	**$Cu(OAc)_2·H_2O$**	***t*AmOH**	**74**
3	$Cu(OAc)_2·H_2O$	H_2O	22
4	$Cu(OAc)_2·H_2O$	DMF	45
5	$Cu(OAc)_2·H_2O$	toluene	56
6	$Cu(OAc)_2·H_2O$	*p*-xylene	56
7	$Cu(OAc)_2·H_2O$	DCE	trace
8	AgOAc	*t*AmOH	trace
9	Ag_2CO_3	*t*AmOH	trace
10	$Cu(OAc)_2·H_2O$	*n*BuOH	57
11	$Cu(OAc)_2·H_2O$	*t*BuOH	68
12	$Cu(OAc)_2·H_2O$	*t*AmOH	54[d]
13	–	*t*AmOH	trace
14	$Cu(OAc)_2·H_2O$	*t*AmOH	74[e]
15	$Cu(OAc)_2·H_2O$	*t*AmOH	22[f]
16	$Cu(OAc)_2·H_2O$ (catalyst: 5.0 mol % $cpRuCl(PPh_3)_2$)	*t*AmOH	16
17	$Cu(OAc)_2·H_2O$ (catalyst: 5.0 mol % $Ru_3(CO)_{12}$)	*t*AmOH	trace
18	$Cu(OAc)_2·H_2O$ (30 mol % KOAc used as additive)	*t*AmOH	27

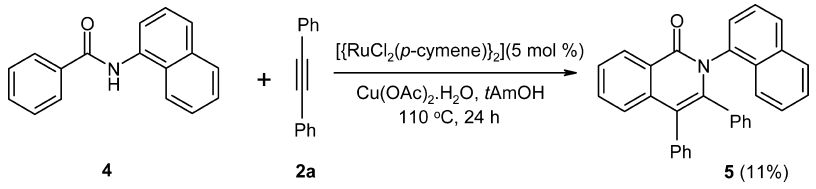
[a]Reaction conditions: amide (0.4 mmol), alkyne (0.8 mmol), oxidant (0.8 mmol), solvent (2 mL), 110 °C (oil bath temperature). [b]Isolated yields. [c]1.5 equiv of alkyne used. [d]2.5 mol % catalyst used. [e]In open air. [f]0.5 equiv of $Cu(OAc)_2·H_2O$ used.

other solvents like H_2O, DMF, toluene, xylene, DCE, BuOH did not improve the yield (entries 3–7, 10, 11). Product formation was not observed when Ag(I) salts were used instead of $Cu(OAc)_2·H_2O$ as the oxidant (entries 8–9). Lower yield of the product was observed when the catalyst loading was decreased to 2.5 mol % (entry 12). A control experiment showed that $Cu(OAc)_2·H_2O$ was necessary for the reaction (entry 13). It is noteworthy that under the same catalytic conditions in *open air* also the reaction afforded the same amount of the product (74%) (entry 14). Rather surprisingly, when we used atmospheric oxygen as an oxidant along with $Cu(OAc)_2·H_2O$ (0.5 equiv), only 22% of the product was observed (entry 15). We have screened other ruthenium complexes like $Ru_3(CO)_{12}$ or $CpRuCl(PPh_3)_2$, we did not get good yield (entries 16–17). When KOAc was used as additive along with $Cu(OAc)_2·H_2O$, lower yield of the product was observed.

Under the above catalytic conditions, the structurally similar, but monodentate directing group naphthyl substituted benzamide (**4**) gave the isoquinolone derivative in very poor yield (11%) (Scheme 1). This result suggests that 8-aminoquinoline (bidentate chelation) is necessary for completion of the reaction.

With the optimization conditions in hand, we investigated the substrate scope with *N*-quinolin-8-yl-benzamides (**1a–p**) and a variety of internal alkynes (**2a–n**). Gratifyingly, in all the cases good to excellent yields of the isoquinolone products were obtained (Scheme 2, Table 2, compounds **3** and **6–37**). The structure of the isoquinolone **3** was confirmed by X-ray crystallography. The reaction works well with both electron-rich (4-Me, 4-OMe, 3,5-Me) and electron-deficient (4-Cl, 4-CF_3) symmetrical arylalkynes, affording the isoquinolone derivatives (**6–10**) in 66–79% yields. Heteroaryl alkynes were tolerated under the catalytic conditions, and the corresponding isoquinolone **11** was formed in good yield (63%). It was also found that dialkylacetylenes reacted smoothly with amide **1a**. When the reaction was performed with 3-hexyne or 4-octyne, the corresponding oxidative cycloaddition products [**12**, **13** (X-ray)] were obtained in good yields (60%, 63%). When unsymmetrical phenyl(alkyl) alkynes were used, interestingly, only one isomer was obtained in a highly *regioselective* manner. Thus, the reaction of amide **1a** with alkynes 1-phenyl-1-pentyne (**2j**), 1-phenyl-1-butyne (**2k**), or 1-phenyl-1-propyne (**2l**) afforded the products **14–16**, which contain the C-aryl carbon adjacent to amide nitrogen, in good yields (62–72%). The regioselectivity of the product was further confirmed by X-ray crystallography for compound **16**. These results suggest that there might be pi–pi stacking directing the observed regioselectivity in the products. However, the selectivity was less significant when 1-(4-nitrophenyl)-2-(4-tolyl)acetylene (**2m**) was used; the major isomer (**17**; X-ray), though, was the one with the C-nitrophenyl group adjacent to amide nitrogen. In the case of usymmetrical dialkylacetylene (*n*-hexyl)C≡CMe (**2n**), isomeric products (**37**) in the ratio 7:3 were observed, thus showing less selectivity. We also attempted reactions using the terminal alkyne, phenylacetylene. However, in this case, only dialkyne product was obtained by self-coupling. Substituted benzamides (**1b–p**) with diphenylacetylene (**2a**) behaved similarly to afford the isoquinolones **19–32** in good yields (61–78%). This oxidative annulation process took place in a highly regioselective manner when we used *meta*-substituted amides. Thus, the reactions of *meta*-iodo or methyl substituted amides (**1k**, **1l**) reacted smoothly with diphenylacetylene and gave the isoquinolones **28–29** as single regioisomers, in which the less hindered C–H bond was functionalized. The reaction also worked well with *ortho*-substituted amide **1m** or naphthylamide **1n** affording the products **30** (73%) or **31** (64%) in excellent yield. Substitution at the 5-OMe substituted *N*-quinolin-8-yl-benzamide also gave good yield of the corresponding isoquinolone **32**. Extension of this oxidative annulation process to heteroarylamides was

Scheme 1. Oxidative Annulation Reaction Using Naphthyl-Substituted Benzamide



4 2a 5 (11%)

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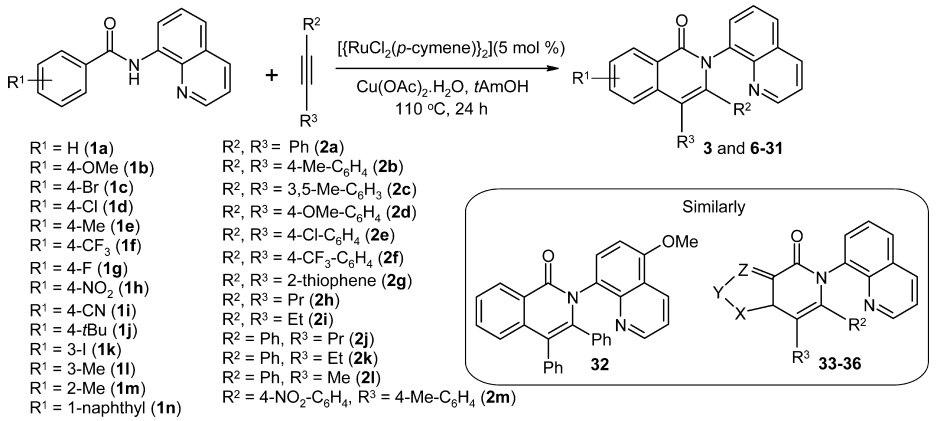
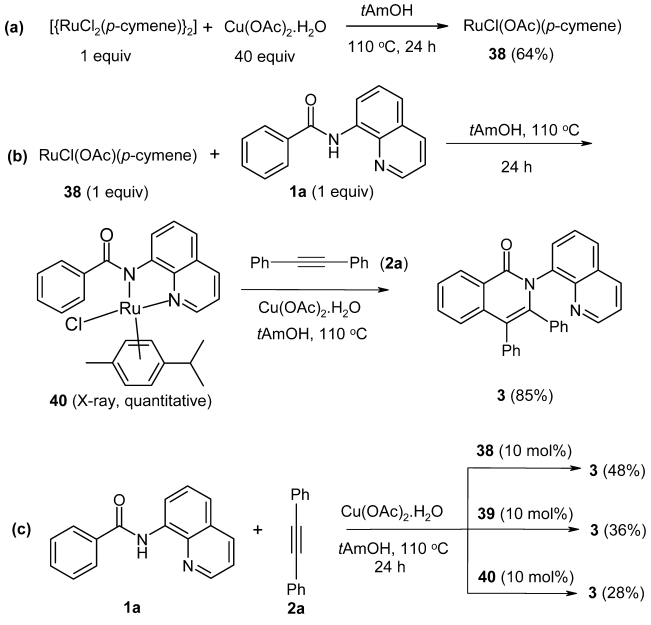
Scheme 2. [Ru]-Catalyzed Reactions of *N*-Quinolin-8-yl-benzamides with Internal Alkynes



successful under the catalytic conditions. 3-Thiopheneamide reacted smoothly with alkyne and furnished the cyclized product **33** in a regioselective manner. Here, the C−H functionalization occurred at the more active 2-position of the thiophene. The 2-substituted heteroamides (thiophenyl, furanyl and indolyl) also reacted well with alkyne and gave the isoquinolone derivatives **34**−**36** in decent yields (51−61%).

What Are the Intermediates? For more information on the reaction pathway, we have conducted some step by step reactions (Scheme 3). The reaction of $[\{RuCl_2(p\text{-cymene})\}_2]$ (1.0 equiv) with $Cu(OAc)_2{\cdot}H_2O$ (40.0 equiv) under reflux conditions in *t*AmOH afforded the monoacetate complex $[RuCl(OAc)(p\text{-cymene})]$ (**38**) and not the bis(acetate) complex $[Ru(OAc)_2(p\text{-cymene})]$ (**39**) (Scheme 3a). Previously, Požgana and Dixneuf had prepared the latter complex by reacting $[\{RuCl_2(p\text{-cymene})\}_2]$ with 4 mol equiv of KOAc in NMP.[14a] Thus, there appears to be difference in the reactivity of $[\{RuCl_2(p\text{-cymene})\}_2]$ under these two conditions. In a further step, the reaction between the monoacetate complex **38** with an equimolar quantity of amide **1a** in stoichiometric amounts in *t*AmOH under reflux conditions yielded the ruthenium complex **40** in quantitative yield (Scheme 3b). The same complex **40** was also obtained by treating the *N*-quinolin-8-yl-benzamide **1a** with $\{RuCl_2(p\text{-cymene})\}_2$ albeit in 52% yield; the yield was better in the presence of NaOAc. In this complex **40**, ruthenium is coordinated to the *N*-quinolin-8-yl-benzamidyl moiety in a *N*,*N*-fashion. There was no indication to suggest the replacement of second chlorine by acetate under these conditions or even after 36 h. Treatment of chloro ligated ruthenium complex **40** with $Cu(OAc)_2{\cdot}H_2O$ in *t*AmOH resulted in some unidentified products, but in the presence of stoichiometric amount of alkyne **2a**, it directly afforded the isoquinolone derivative **3** in 85% yield. In the absence of $Cu(OAc)_2{\cdot}H_2O$ this annulation reaction did not proceed. However, we found that use of **40** (10 mol %) as a catalyst did not perform that well and only ca. 28% yield of the product was obtained. It should be noted here that in both cases the amount of ruthenium metal was the same. We have also checked the catalytic activity of the mono and bis-acetate ruthenium complexes. Both of these complexes show very poor activity and result in low yields of **3** (Scheme 3c). It may be noted that similar reactions using 2-pyridinylmethylamine in the presence of $Ni(cod)_2$ as the catalyst has been reported before.[13] The latter catalyst is air-sensitive, while $\{RuCl_2(p\text{-cymene})\}_2$ is air-stable. In addition, the reaction using $Ni(cod)_2$ had to be conducted in a glovebox, while our ruthenium catalyzed reaction is conducted in open air.

Scheme 3. Preliminary Experiments to Know the Reaction Pathway



On the basis of the above experiments and previous mechanistic insight,[11h,15] we propose a plausible reaction pathway shown in Scheme 4. First, $[RuCl_2(p\text{-cymene})]_2$ undergoes ligand exchange with $Cu(OAc)_2$ to give the monoacetate species $RuCl(OAc)(p\text{-cymene})$ (**38**), which undergoes coordination of nitrogen atom of the quinoline moiety and the oxidative addition of the N−H bond giving the metal complex **40**. Then in the presence of $Cu(OAc)_2$ and alkyne, complex **40** undergoes ligand exchange with the acetate ion to lead to (**I**). This is followed by C−H activation through the elimination of AcOH, forming the five membered matallacycle intermediate **II**. The oxidative addition of alkyne to **II** generates the intermediate **III**. Then reductive elimination gives compound **3** and the active catalyst is regenerated. The only disconcerting point here is that on its own, **40** is not very active as a catalytic intermediate.

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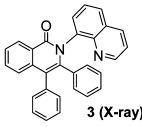
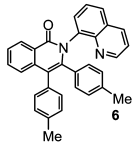
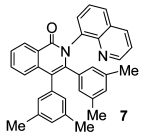
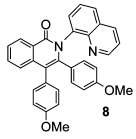
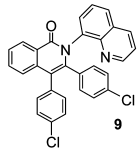
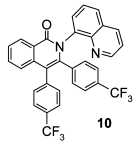
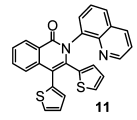
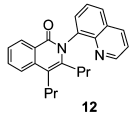
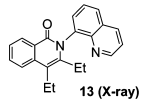
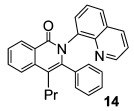
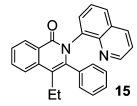
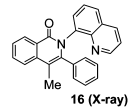
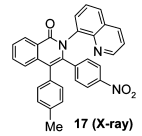
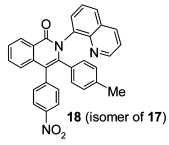
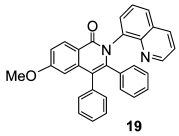
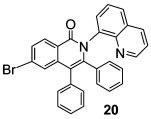
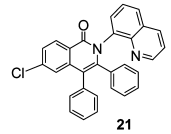
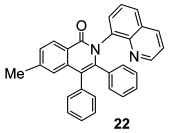
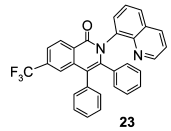
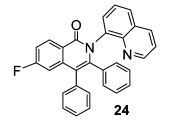
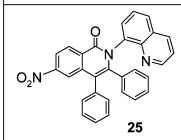
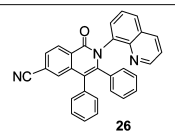
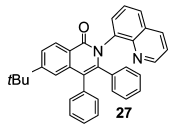
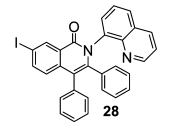
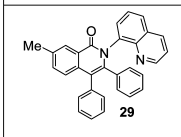
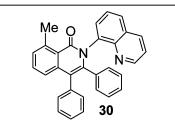
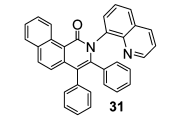
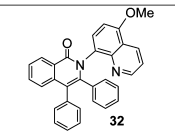
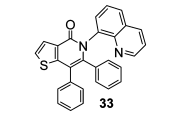
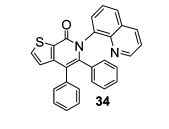
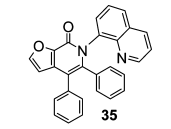
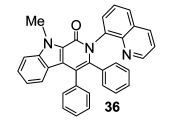
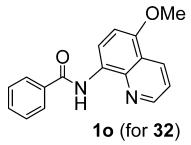
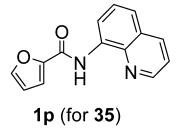
Table 2. Substituted Isoquinolones Synthesized in This Study by C−H Functionalization[a]

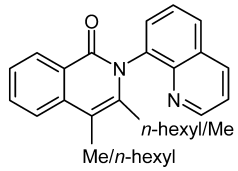
Product	Yield (%)[b]	Product	Yield (%)[b]
 **3 (X-ray)**	74	 **6**	70
 **7**	72	 **8**	71
 **9**	79	 **10**	66
 **11**	63	 **12**	60
 **13 (X-ray)**	63	 **14**	72
 **15**	62	 **16 (X-ray)**	62
 **17 (X-ray)**	34[c] [64% including **18**]	 **18** (isomer of **17**)	28[c] [64% including **17**]
 **19**	71	 **20**	68

Product	Yield (%)[b]	Product	Yield (%)[b]
 **21**	78	 **22**	74
 **23**	65	 **24**	71
 **25**	72	 **26**	72
 **27**	74	 **28**	61
 **29**	67	 **30**	73
 **31**	64	 **32**	64[d]
 **33**	62	 **34**	51
 **35**	56[d]	 **36**	61

[a]Reaction conditions: amide (0.4 mmol), alkyne (0.8 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (5 mol %)/$Cu(OAc)_2 \cdot H_2O$ (0.8 mmol), *t*AmOH (2 mL), 110 °C (oil bath temperature), in open air, 24 h. [b]Isolated yield. [c]Combined yield (**17** + **18**). [d]Amide used was


1o (for **32**)


1p (for **35**)


Me/*n*-hexyl
37 (isomer ratio ~ 7:3)

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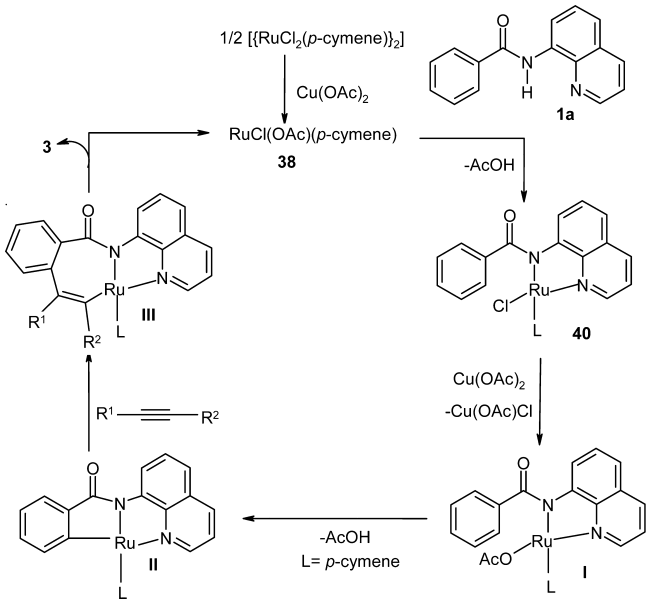
Scheme 4. Plausible Reaction Pathway for the Formation of 3 (and 6−37)



CONCLUSIONS

In summary, we have developed an efficient method for the synthesis of isoquinolones via the oxidative annulation of *N*-quinolin-8-yl-benzamides with alkynes with the aid of 8-aminoquinoline as bidentate directing group in the presence of Ru-catalyst in open air. The reaction features a high regioselectivity, good substrate scope, and large functional group tolerance. We have also successfully extended this method to heterocyclic amides. A ruthenium *N*-quinolin-8-yl-benzamide complex is isolated and characterized, showing the key role played by the quinoline moiety. Further synthetic applications of directing group methodology and mechanistic studies may reveal many more useful transformations.

EXPERIMENTAL SECTION

General Comments. Solvents were dried according to known methods as appropriate.[16] ^{1}H, ^{13}C spectra (^{1}H, 400 MHz; ^{13}C, 100 MHz) were recorded using a 400 MHz spectrometer in $CDCl_3$ with shifts referenced to $SiMe_4$ (δ = 0). IR spectra were recorded on an FTIR spectrophotometer. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. Elemental analyses were carried out on a CHN analyzer. Mass spectra were recorded using LC−MS and HRMS (ESI-TOF analyzer) equipment.

(i). Synthesis of Precursor Amides 1a−1p and 4. All the amide precursors bearing 8-aminoquinoline moiety were prepared by the reaction of corresponding acid chlorides with 8-aminoquinoline according to the literature procedures.[17] Compounds **1a−1n** and **4** are known. Compounds **1o** and **1p** are new.

Compound ***1o***. Yield 1.126 g (81%, yellow solid): mp 120−124 °C; IR (KBr, cm^{-1}) 3375, 2981, 1677, 1551, 1496, 1397, 1282, 1151, 1085, 827, 784, 679; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (br s, 1H), 8.88 (s, 2H), 8.86 (s, 1H), 8.61 (dd, J = 8.4 and 1.6 Hz, 1H), 8.09−8.07 (m, 1H), 7.58−7.55 (m, 3H), 7.47 (dd, J = 8.4 and 1.6 Hz, 1H), 6.90 (d, J = 8.8 Hz, 1H), 4.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 150.5, 148.8, 139.6, 135.5, 131.7, 131.4, 128.8, 128.1, 127.3, 120.9, 120.6, 116.8, 104.5, 55.9; LC−MS m/z 279 [M + 1]$^+$. Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.51; H, 5.16; N, 10.15.

Compound ***1p***. Yield 0.940 g (79%, yellow solid): mp 138−142 °C; IR (KBr, cm^{-1}) 3326, 1682, 1595, 1545, 1332, 1156, 1008, 871, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (br s, 1H), 8.89−8.87 (m, 2H), 8.17 (d, J = 8.4 Hz, 1H), 7.63 (s, 1H), 7.58−7.53 (m, 2H), 7.47 (dd, J ∼ 8.2 and 4.2 Hz, 1H), 7.31 (d, J = 3.2 Hz, 1H), 6.59−6.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 148.5, 144.6, 138.7, 136.4, 134.3, 128.1, 127.5, 121.9, 121.8, 116.7, 115.2, 112.5; LC−MS m/z 239 [M + 1]$^+$. Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.46; H, 4.27; N, 11.65.

(ii). General Procedure for the Ruthenium-Catalyzed Coupling of *N*-Quinolin-8-yl-benzamides with Alkynes: Synthesis of Compounds 3 and 5−37. A mixture of *N*-quinolin-8-yl-benzamide or naphthyl benzamide (0.4 mmol), diphenylacetylene (0.8 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), and $Cu(OAc)_2{\cdot}H_2O$ (0.8 mmol) was taken in a Schlenk tube [under ambient conditions; no inert atmosphere needed]. To this, *t*AmOH (2 mL) was added, and the mixture was stirred at 110 °C (oil bath temperature) for 24 h. After cooling to rt, saturated NH_4Cl solution (50 mL) was added, and the contents were extracted with EtOAc (3 × 30 mL). The combined organic phase was washed with brine solution (30 mL), dried over anh. Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane-EtOAc (1:1) mixture as the eluent.

Compound ***3***. Yield 0.127 g (74%, white solid): mp 246−248 °C; IR (KBr, cm^{-1}) 3052, 2926, 1655, 1595, 1490, 1332, 1178, 1030, 816, 784, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 4.0 Hz, 1H), 8.59 (d, J = 7.6 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.61(t, J ∼ 7.6 Hz, 1H), 7.55−7.49 (m, 2H), 7.40−7.36 (m, 2H), 7.32 (d, J = 8.0 Hz, 1H), 7.27−7.25 (m, 2H), 7.18−7.16 (m, 3H), 6.98 (d, J = 7.6 Hz, 1H), 6.84 (t, J = 7.6 Hz, 1H), 6.76−6.71 (m, 2H), 6.50 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 150.8, 144.7, 141.9, 138.2, 137.7, 136.6, 136.1, 134.9, 132.5, 131.9, 131.7, 130.9, 130.8, 129.8, 128.8, 128.6, 128.5, 128.1, 127.8, 127.3, 126.8, 126.7, 126.5, 125.8, 125.7, 121.5, 118.6; HRMS (ESI) Calcd for $C_{30}H_{21}N_2O$ [M$^+$ + H] m/z 425.1655, found 425.1656. X-ray structure was determined for this compound.

Compound ***5***. Yield 0.018 g (11%, white solid): mp 200−204 °C; IR (KBr, cm^{-1}) 3057, 2926, 1649, 1610, 1484, 1440, 1397, 1254, 1029, 914, 777; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.72 (d, J ∼ 8.2 Hz, 1H), 7.69−7.63 (m, 2H), 7.59−7.56 (m, 1H), 7.52−7.43 (m, 2H), 7.35−7.28 (m, 2H), 7.26−7.24 (m, 3H), 7.19−7.14 (m, 3H), 7.00 (d, J = 7.6 Hz, 1H), 6.86 (t, J ∼ 7.4 Hz, 1H), 6.75 (t, J ∼ 7.4 Hz, 1H), 6.61 (d, J = 7.6 Hz, 1H), 6.54−6.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 142.0, 138.0, 136.4, 134.5, 134.0, 132.8, 131.8, 131.7, 131.1, 131.0, 129.5, 128.6$_4$, 128.5$_6$, 128.4, 128.1, 128.0, 127.9, 127.4, 127.1, 127.0, 126.8, 126.7, 126.2, 125.8, 125.6, 125.0, 123.0, 119.2; HRMS (ESI) Calcd for $C_{31}H_{22}NO$ [M$^+$ + H] m/z 424.1702, found 424.1701.

Compound ***6***. Yield 0.128 g (70%, white solid): mp 278−282 °C; IR (KBr, cm^{-1}) 3014, 2909, 1660, 1507, 1337, 1178, 1025, 899, 734; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 2.8 Hz, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.59 (t, J ∼ 7.6 Hz, 1H), 7.53−7.46 (m, 2H), 7.39−7.36 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 8.0 Hz, 1H), 7.05 (t, J = 7.2 Hz, 2H), 6.98 (d, J = 8.0 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 6.63 (t, J ∼ 7.8 Hz, 2H), 6.29 (d, J = 7.6 Hz, 1H), 2.28 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 150.7, 144.8, 142.0, 138.5, 137.9, 136.7, 136.1, 133.7, 132.4, 132.1, 131.7, 131.5, 130.9, 130.7, 129.6, 128.8, 128.5$_3$, 128.4$_7$, 128.4, 127.4, 127.2, 126.5, 125.8, 125.7, 125.6, 121.5, 118.6, 21.3, 21.1; HRMS (ESI) Calcd for $C_{32}H_{25}N_2O$ [M$^+$ + H] m/z 453.1968, found 453.1968.

Compound ***7***. Yield 0.139 g (72%, white solid): mp 268−272 °C; IR (KBr, cm^{-1}) 2920, 1649, 1589, 1556, 1474, 1326, 1222, 1025, 833, 795, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 2.4 Hz, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.51 (t, J ∼ 7.4 Hz, 1H), 7.45 (d, J = 7.2 Hz, 1H), 7.38−7.31 (m, 3H), 6.91 (br s, 1H), 6.78 (br s, 2H), 6.57 (br s, 1H), 6.33 (d, J = 8.4 Hz, 2H), 2.25 (s, 3H), 2.15 (s, 3H), 1.97 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 150.6, 145.0, 142.0, 138.4, 138.0, 137.2, 136.8, 136.4, 135.9, 135.6, 135.5, 134.7, 132.3, 130.8, 129.7, 129.5, 128.7, 128.6, 128.4,

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128.3$_2$, 128.2$_5$, 127.8, 126.4, 125.8, 125.7, 125.5, 121.3, 118.5, 21.3, 21.2, 20.9, 20.5; HRMS (ESI) Calcd for $C_{34}H_{29}N_2O$ [M$^+$ + H] m/z 481.2281, found 481.2279.

Compound **8**. Yield 0.138 g (71%, white solid): mp 236−240 °C; IR (KBr, cm^{-1}) 3052, 2986, 1660, 1611, 1507, 1474, 1326, 1244, 1184, 1025, 893, 816; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, J = 2.8 Hz, 1H), 8.57 (d, J = 7.6 Hz, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.53−7.47 (m, 2H), 7.41−7.36 (m, 2H), 7.32 (d, J = 8.4 Hz, 1H), 7.15 (dd, J = 8.4 and 1.6 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 6.88−6.86 (m, 1H), 6.80 (dd, J = 8.4 and 2.4 Hz, 1H), 6.73 (dd, J = 8.4 Hz and J = 2.4 Hz, 1H), 6.67−6.65 (m, 1H), 6.38 (dd, J = 8.8 Hz and J = 2.4 Hz, 1H), 6.03 (dd, J = 8.4 Hz and $J \sim$ 2.2 Hz, 1H), 3.76 (s, 3H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 158.2, 150.7, 144.8, 141.9, 138.6, 137.9, 136.1, 132.9, 132.7, 132.4, 132.0, 131.0, 130.9, 129.0, 128.8, 128.5, 128.4, 127.6, 126.5, 125.9, 125.7, 121.5, 118.4, 113.5, 113.4, 112.1, 112.0, 55.1, 54.8; HRMS (ESI) Calcd for $C_{32}H_{25}N_2O_3$ [M$^+$ + H] m/z 485.1866, found 485.1864.

Compound **9**. Yield 0.156 g (79%, white solid): mp 282−286 °C; IR (KBr, cm^{-1}) 2921, 1649, 1595, 1490, 1403, 1326, 1145, 1096, 1014, 893, 822, 784, 603; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, J = 2.4 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.11−8.08 (m, 1H), 7.73−7.71 (m, 1H), 7.63−7.61 (m, 1H), 7.57−7.50 (m, 2H), 7.44−7.38 (m, 2H), 7.25−7.20 (m, 3H), 7.14 (t, $J \sim$ 7.0 Hz, 2H), 6.91−6.84 (m, 2H), 6.71 (dd, J = 8.4 and 1.2 Hz, 1H), 6.52−6.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.9, 144.6, 140.9, 137.7, 137.3, 136.2, 134.9, 133.5, 133.2, 133.1$_4$, 133.0$_8$, 132.9, 132.7, 132.0, 131.1, 130.9, 129.0, 128.9, 128.6, 128.4, 127.2, 127.1, 127.0, 125.9, 125.7, 125.4, 121.7, 117.6; HRMS (ESI) Calcd for $C_{30}H_{19}Cl_2N_2O$ [M$^+$ + H] 493.0875, found m/z 493.0873, 495.0841 and 497.0816.

Compound **10**. Yield 0.149 g (66%, white solid): mp 262−266 °C; IR (KBr, cm^{-1}) 3057, 1660, 1611, 1485, 1321, 1173, 1107, 1063, 827, 679; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, J = 4.0 Hz, 1H), 8.60 (d, J = 7.6 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.67−7.57 (m, 2H), 7.54−7.52 (m, 2H), 7.48 (d, J = 8.4 Hz, 1H), 7.43−7.39 (m, 2H), 7.34 (t, $J \sim$ 8.2 Hz, 2H), 7.21 (d, J = 8.0 Hz, 1H), 7.12 (t, J = 9.2 Hz, 2H), 6.93 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 151.0, 144.5, 140.7, 140.1, 138.1, 137.3, 137.0, 136.3, 132.9, 132.2, 132.0, 131.1, 131.0, 130.3, 129.8, 129.6, 129.5, 129.2, 129.0, 128.7, 127.4, 125.9, 125.4, 125.1, 124.8, 123.9, 123.6, 122.1, 121.8, 117.5; HRMS (ESI) Calcd for $C_{32}H_{19}F_6N_2O$ [M$^+$ + H] m/z 561.1402, found 561.1401.

Compound **11**. Yield 0.110 g (63%, white solid): mp 248−252 °C; IR (KBr, cm^{-1}) 3063, 1660, 1600, 1479, 1321, 1249, 1145, 833, 805, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 2.8 Hz, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.69−7.65 (m, 1H), 7.58−7.52 (m, 3H), 7.47−7.40 (m, 2H), 7.27 (br s, 1H), 6.97−6.94 (m, 2H), 6.85 (d, J = 4.8 Hz, 1H), 6.48 (d, J = 2.8 Hz, 1H), 6.35 (dd, J = 3.6, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 151.0, 144.8, 138.1, 137.4, 137.2, 137.0, 136.3, 134.9, 132.8, 130.6, 130.0, 128.9, 128.4, 127.5, 127.2, 126.6, 126.0, 125.9, 125.8, 125.3, 121.7, 114.0; HRMS (ESI) Calcd for $C_{26}H_{17}N_2OS_2$ [M$^+$ + H] m/z 437.0783, found 437.0784.

Compound **12**. Yield 0.086 g (60%, white solid): mp 122−126 °C; IR (KBr, cm^{-1}) 3063, 2959, 1655, 1551, 1496, 1370, 1326, 882, 833, 795, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, J = 4.0 Hz, 1H), 8.46 (d, J = 8.0 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.76−7.66 (m, 4H), 7.46−7.41 (m, 2H), 2.80−2.75 (m, 2H), 2.51−2.45 (m, 1H), 1.98−1.90 (m, 1H), 1.77−1.70 (m, 2H), 1.39−1.29 (m, 2H), 1.12 (t, $J \sim$ 7.4 Hz, 3H), 0.54 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 151.3, 144.9, 141.0, 137.7, 137.6, 136.3, 132.4, 130.4, 129.3, 129.1, 128.7, 126.2, 125.7, 125.6, 123.0, 121.8, 113.6, 32.8, 30.0, 23.7, 23.1, 14.6, 14.2; HRMS (ESI) Calcd for $C_{24}H_{25}N_2O$ [M$^+$ + H] m/z 357.1968, found 357.1967.

Compound **13**. Yield 0.083 g (63%, white solid): mp 190−194 °C; IR (KBr, cm^{-1}) 3074, 2975, 1654, 1588, 1495, 1331, 1216, 1057, 832, 783, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88−8.87 (m, 1H), 8.46 (d, J = 8.0 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.74−7.67 (m, 3H), 7.47−7.42 (m, 2H), 2.91−2.85 (m, 2H), 2.61−2.55 (m, 1H), 2.12−2.06 (m, 1H), 1.34 (t, $J \sim$ 7.4 Hz, 3H), 0.89 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 151.4, 144.9, 141.8, 137.5, 136.4, 132.5, 130.7, 130.4, 129.4, 129.2, 128.8, 126.3, 125.7, 125.6, 122.9, 121.9, 114.8, 23.7, 20.7, 15.0, 14.1; HRMS (ESI) Calcd for $C_{22}H_{21}N_2O$ [M$^+$ + H] m/z 329.1655, found 329.1654. X-ray structure was determined for this compound.

Compound **14**. Yield 0.113 g (72%, white solid): mp 144−148 °C; IR (KBr, cm^{-1}) 3052, 2921, 2866, 1655, 1611, 1562, 1490, 1332, 1030, 822, 795, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90−8.89 (m, 1H), 8.58 (d, J = 7.6 Hz, 1H), 8.04 (dd, $J \sim$ 7.8 Hz and ∼1.4 Hz, 1H), 7.83−7.75 (m, 2H), 7.64 (d, J = 8.0 Hz, 1H), 7.54 (t, $J \sim$ 7.6 Hz, 1H), 7.46−7.44 (m, 1H), 7.38−7.34 (m, 2H), 7.19 (d, J = 7.6 Hz, 1H), 7.12 (d, $J \sim$ 7.4 Hz, 1H), 6.97 (t, $J \sim$ 7.4 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 6.72 (t, $J \sim$ 7.4 Hz, 1H), 2.49−2.43 (m, 2H), 1.63−1.59 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 150.7, 144.7, 141.1, 137.9, 137.4, 136.0, 135.2, 132.5, 131.0, 130.3, 129.2, 128.9, 128.7, 128.4, 127.8, 127.2, 127.0, 126.4, 126.3, 125.7, 123.6, 121.4, 115.1, 30.7, 23.7, 14.4; HRMS (ESI) Calcd for $C_{27}H_{23}N_2O$ [M$^+$ + H] m/z 391.1811, found 391.1809.

Compound **15**. Yield 0.094 g (62%, white solid): mp 178−182 °C; IR (KBr, cm^{-1}) 2959, 1649, 1611, 1490, 1332, 1151, 1074, 816, 784, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, J = 2.8 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.78 (t, $J \sim$ 7.4 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.45 (d, J = 6.4 Hz, 1H), 7.38−7.34 (m, 2H), 7.20 (d, J = 7.2 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.98 (t, $J \sim$ 7.4 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.73 (t, $J \sim$ 7.4 Hz, 1H), 2.59−2.50 (m, 2H), 1.15 (t, $J \sim$ 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 150.8, 144.7, 140.9, 137.9, 137.1, 136.0, 135.3, 132.5, 131.0, 130.2, 129.1, 129.0, 128.8, 128.5, 127.8, 127.4, 127.1, 126.5, 125.8, 123.6, 121.5, 116.3, 21.7, 14.9; HRMS (ESI) Calcd for $C_{26}H_{21}N_2O$ [M$^+$ + H] m/z 377.1655, found 377.1656.

Compound **16**. Yield 0.091 g (62%, white solid): mp 186−190 °C; IR (KBr, cm^{-1}) 2921, 1655, 1616, 1485, 1332, 1145, 899, 789, 756, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, J = 2.8 Hz, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.05 (dd, J = 8.4 and 1.2 Hz, 1H), 7.83−7.76 (m, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.56 (t, $J \sim$ 7.4 Hz, 1H), 7.44 (d, J = 6.8 Hz, 1H), 7.38−7.34 (m, 2H), 7.19−7.12 (m, 2H), 6.98 (t, $J \sim$ 7.4 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.74 (t, $J \sim$ 7.4 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.9, 144.8, 140.9, 138.2, 138.0, 136.0, 135.5, 132.7, 131.0, 130.4, 129.3, 128.7, 128.5, 127.8, 127.4, 127.2, 126.6, 126.0, 125.8, 123.6, 121.5, 110.3, 14.9; HRMS (ESI) Calcd for $C_{25}H_{19}N_2O$ [M$^+$ + H] m/z 363.1498, found 363.1498. X-ray structure was determined for this compound.

Compound **17**. Yield 0.067g (34%, combined yield along with **18** was 62%, yellow solid): mp >300 °C; IR (KBr, cm^{-1}) 3052, 1655, 1589, 1523, 1479, 1348, 1107, 822, 789, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (dd, J = 4.0 and 1.6 Hz, 1H), 8.60−8.58 (m, 1H), 8.09 (dd, $J \sim$ 8.2 and 1.4 Hz, 1H), 7.73−7.70 (m, 2H), 7.66−7.62 (m, 1H), 7.59−7.55 (m, 2H), 7.44−7.37 (m, 3H), 7.33 (d, J = 8.0 Hz, 1H), 7.17 (dd, J = 8.4 and 1.6 Hz, 1H), 7.08−7.06 (m, 3H), 7.03−6.99 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 151.0, 146.4, 144.4, 141.8, 139.4, 137.9, 137.1, 136.3, 132.7, 132.5, 131.7, 131.5, 131.3, 131.1, 130.9, 129.2, 129.1, 129.0, 128.9, 128.5, 127.3, 125.9, 125.8, 121.9, 121.8, 121.7, 118.9, 21.2; HRMS (ESI) Calcd for $C_{31}H_{22}N_3O_3$[M$^+$ + H] 484.1662, found 484.1665. X-ray structure was determined for this compound.

Compound **18**. Yield 0.055 g (28%, combined yield along with **17** was 62%, yellow solid): mp 292−296 °C; IR (KBr, cm^{-1}) 3063, 1655, 1589, 1507, 1342, 1189, 1151, 1019, 805, 712; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 2.8 Hz, 1H), 8.60 (d, J = 7.6 Hz, 1H), 8.13−8.04 (m, 3H), 7.70 (d, J = 8.0, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.56 (t, $J \sim$ 7.4 Hz, 1H), 7.49 (d, J = 6.8 Hz, 1H), 7.44−7.36 (m, 4H), 7.20 (d, J = 8.0 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 6.66 (d, J = 7.6 Hz, 1H), 6.60 (d, J = 8.0 Hz, 1H), 6.32 (d, J = 7.6 Hz, 1H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.8, 146.6, 144.7,

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144.4, 142.7, 137.6, 137.4, 137.1, 136.1, 132.9, 132.8, 132.7, 131.2, 130.8, 130.4, 129.5, 128.8, 127.8, 127.6, 127.1, 125.8, 125.6, 124.8, 123.4, 123.1, 121.6, 116.5, 21.1; HRMS (ESI) Calcd for $C_{31}H_{22}N_3O_3$[M$^+$ + H] 484.1662, found 484.1657.

Compound ***19***. Yield 0.128 g (71%, white solid): mp 280−284 °C; IR (KBr, cm^{-1}) 2926, 1649, 1611, 1485, 1381, 1332, 1227, 1030, 937, 849, 784, 723; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, J = 8.4 and 1.6 Hz, 1H), 8.51 (d, J = 8.8 Hz, 1H), 8.06 (dd, J = 8.4 and 1.6 Hz, 1H), 7.67−7.65 (m, 1H), 7.51−7.49 (m, 1H), 7.39−7.35 (m, 2H), 7.24−7.21 (m, 2H), 7.18−7.10 (m, 4H), 6.97 (d, J = 7.6 Hz, 1H), 6.83 (t, J = 7.6 Hz, 1H), 6.76−6.70 (m, 2H), 6.68 (d, J = 2.4 Hz, 1H), 6.49 (t, J = 7.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 162.5, 150.8, 144.9, 142.6, 140.3, 137.8, 136.7, 136.1, 135.1, 131.9, 131.7, 131.1, 130.8, 130.7, 129.8, 128.8, 128.6, 128.1, 127.9, 127.2, 126.8, 126.7, 126.5, 125.8, 121.5, 119.6, 118.3, 115.4, 107.7, 55.4; HRMS (ESI) Calcd for $C_{31}H_{23}N_2O_2$ [M$^+$ + H] m/z 455.1760, found 455.1757.

Compound ***20***. Yield 0.137 g (68%, white solid): mp 294−298 °C; IR (KBr, cm^{-1}) 3058, 2921, 1655, 1589, 1468, 1315, 1151, 1074, 1019, 904, 816, 784, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 4.0 Hz, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.50−7.45 (m, 2H), 7.40−7.36 (m, 2H), 7.24−7.17 (m, 5H), 6.96 (d, J = 7.6 Hz, 1H), 6.84 (t, J ∼ 7.4 Hz, 1H), 6.73 (t, J ∼ 8.0 Hz, 2H), 6.50 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 150.9, 144.6, 143.4, 139.8, 137.4, 136.1, 135.8, 134.6, 131.8, 131.6, 130.8, 130.6, 130.3, 130.0, 129.7, 128.8, 128.3, 128.1$_3$, 128.0$_8$, 128.0, 127.4, 127.1, 126.8, 126.5, 125.8, 124.3, 121.6, 117.6; HRMS (ESI) Calcd for $C_{30}H_{20}BrN_2O$ [M$^+$ + H] m/z 503.0760 and 503.0740, found 503.0761 and 505.0744.

Compound ***21***. Yield 0.137 g (78%, white solid): mp 284−288 °C; IR (KBr, cm^{-1}) 2921, 1649, 1595, 1496, 1463, 1321, 1085, 1030, 910, 827, 784, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 2.8 Hz, 1H), 8.51 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.48 (t, J ∼ 7.2 Hz, 2H), 7.40−7.36 (m, 2H), 7.23−7.17 (m, 6H), 6.96 (d, J = 8.0 Hz, 1H), 6.84 (t, J ∼ 7.4 Hz, 1H), 6.73 (t, J = 7.6 Hz, 2H), 6.50 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 150.9, 144.6, 143.4, 139.6, 139.2, 137.4, 136.1, 135.9, 134.6, 131.8, 131.6, 130.8, 130.6, 130.3, 129.7, 128.8, 128.3, 128.1, 127.4, 127.2, 127.1, 126.8, 126.5, 125.8, 125.0, 124.0, 121.6, 117.8; HRMS (ESI) Calcd for $C_{30}H_{20}ClN_2O$ [M$^+$ + H] m/z 459.1265 and 461.1232, found 459.1262 and 461.1237.

Compound ***22***. Yield 0.132 g (74%, white solid): mp 270−274 °C; IR (KBr, cm^{-1}) 2921, 1649, 1616, 1490, 1447, 1331, 1178, 1025, 816, 789, 723, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, J = 4.0 Hz, 1H), 8.48 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.39−7.35 (m, 3H), 7.24 (br s, 2H), 7.18 (br s, 3H), 7.08 (br s, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.83 (t, J ∼ 7.4 Hz, 1H), 6.75−6.70 (m, 2H), 6.48 (t, J ∼ 7.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.8, 144.8, 143.0, 142.0, 138.3, 137.8, 136.7, 136.0, 135.1, 131.9, 131.7, 130.9, 130.8, 129.8, 128.7, 128.5$_1$, 128.4$_7$, 128.3, 128.0, 127.8, 127.2, 126.7, 126.6, 126.4, 125.8, 125.3, 123.5, 121.5, 118.4, 22.1; HRMS (ESI) Calcd for $C_{31}H_{23}N_2O$ [M$^+$ + H] m/z 439.1811, found 439.1812.

Compound ***23***. Yield 0.127 g (65%, white solid): mp 220−224 °C; IR (KBr, cm^{-1}) 3074, 1660, 1595, 1562, 1496, 1430, 1315, 1173, 1074, 915, 784, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (dd, J = 8.0 and 1.6 Hz, 1H), 8.70 (d, J = 8.4, 1H), 8.08 (dd, J = 8.4 and 1.6 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.59 (br s, 1H), 7.50 (dd, J = 7.2 and 1.2 Hz, 1H), 7.41−7.37 (m, 2H), 7.27−7.19 (m, 5H), 6.98 (d, J = 8.0 Hz, 1H), 6.86 (t, J = 7.6 Hz, 1H), 6.77−6.72 (m, 2H), 6.51 (t, J ∼ 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 150.9, 144.5, 143.6, 138.3, 137.3, 136.1, 135.6, 134.5, 131.7, 131.5, 130.7, 130.6, 129.6$_1$, 129.5$_8$, 128.9, 128.8, 128.4, 128.2, 127.7, 127.6, 127.3, 126.8, 126.6, 125.8, 122.9, 122.7, 121.7, 118.3; HRMS (ESI) Calcd for $C_{31}H_{20}F_3N_2O$ [M$^+$ + H] m/z 493.1528, found 493.1527.

Compound ***24***. Yield 0.126 g (71%, white solid): mp 278−282 °C; IR (KBr, cm^{-1}) 3074, 1660, 1611, 1474, 1370, 1326, 1189, 1112, 948, 866, 822, 789, 729, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, J ∼ 4.2 Hz and ∼1.4 Hz, 1H), 8.59 (dd, J = 8.8 and 2.0 Hz, 1H), 8.08−8.06 (m, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.40−7.36 (m, 2H), 7.28−7.17 (m, 6H), 6.98−6.93 (m, 2H), 6.84 (t, J ∼ 7.8 Hz, 1H), 6.75−6.72 (m, 2H), 6.50 (t, J ∼ 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 (d, J = 250.4 Hz), 162.1, 150.9, 144.7, 143.3, 140.8, 140.7, 137.5, 136.0, 134.7, 131.7, 131.5, 130.8, 130.6, 129.6, 128.7, 128.2, 128.0, 127.4, 127.1, 126.7, 126.5, 125.8, 122.2, 121.6, 118.1, 115.3, 115.1, 111.0, 110.7; HRMS (ESI) Calcd for $C_{30}H_{20}FN_2O$ [M$^+$ + H] m/z 443.1560, found 443.1557.

Compound ***25***. Yield 0.134 g (72%, white solid): mp 264−268 °C; IR (KBr, cm^{-1}) 3052, 1666, 1589, 1529, 1463, 1348, 1173, 1129, 1019, 915, 816, 784, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, J = 4.0 and 1.6 Hz, 1H), 8.74 (d, J = 8.8 Hz, 1H), 8.27 (dd, J ∼ 8.6 Hz and ∼2.2 Hz, 1H), 8.18 (d, J = 1.6 Hz, 1H), 8.09 (dd, J ∼ 8.2 Hz, and J ∼ 1.4 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.51−7.50 (m, 1H), 7.42−7.38 (m, 2H), 7.29−7.19 (m, 5H), 6.98 (d, J = 7.6 Hz, 1H), 6.87 (t, J ∼ 7.4 Hz, 1H), 6.78−6.72 (m, 2H), 6.52 (t, J ∼ 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 151.0, 150.6, 144.5, 144.4, 139.0, 137.0, 136.2, 135.1, 134.2, 131.7, 131.4, 130.6, 130.5, 129.5, 129.2, 129.1, 128.8, 128.6, 128.4, 127.7, 127.6, 126.9, 126.7, 125.8, 121.8, 121.3, 120.3, 118.4; HRMS (ESI) Calcd for $C_{30}H_{20}N_3O_3$ [M$^+$ + H] m/z 470.1505, found 470.1504.

Compound ***26***. Yield 0.129 g (72%, white solid): mp 256−260 °C; IR (KBr, cm^{-1}) 3063, 2921, 2225, 1660, 1616, 1551, 1496, 1474, 1332, 1173, 1019, 893, 789, 718; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93−8.92 (m, 1H), 8.66 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.72−7.68 (m, 2H), 7.65 (s, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.41−7.37 (m, 2H), 7.29−7.27 (m, 1H), 7.22−7.16 (m, 4H), 6.98 (d, J = 7.6 Hz, 1H), 6.86 (t, J ∼ 7.4 Hz, 1H), 6.77−6.72 (m, 2H), 6.51 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 150.9, 144.4, 144.2, 138.5, 137.1, 136.2, 135.2, 134.2, 131.7, 131.4, 130.7, 130.6, 130.5, 129.6, 129.5, 129.0, 128.8, 128.5, 128.3, 128.0, 127.7, 127.5, 126.9, 126.6, 125.8, 121.7, 118.6, 117.7, 116.0; HRMS (ESI) Calcd for $C_{31}H_{20}N_3O$ [M$^+$ + H] m/z 450.1607, found 450.1606.

Compound ***27***. Yield 0.142 g (74%, white solid): mp 262−266 °C; IR (KBr, cm^{-1}) 2948, 1655, 1616, 1479, 1392, 1321, 1184, 1019, 932, 827, 795, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (dd, J ∼ 4.6 Hz and ∼1.8 Hz, 1H), 8.53 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.66−7.60 (m, 2H), 7.50 (d, J = 7.2 Hz, 1H), 7.39−7.32 (m, 3H), 7.26−7.16 (m, 5H), 6.98 (d, J = 7.2 Hz, 1H), 6.85−6.82 (m, 1H), 6.76−6.70 (m, 2H), 6.51−6.47 (m, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 155.9, 150.8, 144.8, 141.8, 138.0, 137.9, 136.7, 136.0, 135.1, 131.9, 131.7, 131.0, 130.9, 129.9, 128.8, 128.5, 128.2, 128.0, 127.7, 127.2, 126.7, 126.6, 125.8, 124.8, 123.4, 121.8, 121.5, 118.9, 35.3, 31.1; HRMS (ESI) Calcd for $C_{34}H_{29}N_2O$ [M$^+$ + H] m/z 481.2281, found 481.2280.

Compound ***28***. Yield 0.135 g (61%, white solid): mp 222−226 °C; IR (KBr, cm^{-1}) 3063, 1654, 1594, 1495, 1473, 1320, 1134, 1073, 1024, 827, 788, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, J = 2.8 Hz, 1H), 8.91 (br s, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.86 (dd, J ∼ 8.6 Hz, and ∼1.8 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.41−7.36 (m, 2H), 7.24−7.20 (m, 2H), 7.16−7.14 (m, 3H), 7.03 (d, J = 8.8 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H), 6.84 (t, J ∼ 7.6 Hz, 1H), 6.75−6.71 (m, 2H), 6.50 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 150.7, 144.2, 142.5, 141.4, 141.2, 137.3, 137.1, 136.8, 135.9, 134.5, 131.7, 131.5, 131.2, 130.7, 129.6, 128.9, 128.2, 127.9, 127.6, 127.5, 127.3, 127.0, 126.8, 126.6, 126.0, 121.7, 118.5, 91.8; HRMS (ESI) Calcd for $C_{30}H_{20}IN_2O$ [M$^+$ + H] m/z 551.0621, found 551.0621.

Compound ***29***. Yield 0.118 g (67%, white solid): mp 274−278 °C; IR (KBr, cm^{-1}) 3052, 2910, 1655, 1595, 1501, 1332, 1200, 1025, 805, 789, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94−8.93 (m, 1H), 8.40 (br s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.39−7.35 (m, 2H), 7.25−7.15 (m, 6H), 6.98 (d, J = 7.2 Hz, 1H), 6.84 (t, J = 7.6 Hz, 1H), 6.75−6.70 (m, 2H), 6.49 (t, J = 7.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.8, 144.8, 140.9, 137.9,

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136.8, 136.0, 135.9, 135.0, 133.9, 131.9, 131.7, 130.9, 129.9, 128.8, 128.5, 128.0, 127.8, 127.2, 126.7$_0$, 126.6$_5$, 126.4, 125.8, 125.7, 125.5, 121.5, 118.5, 21.5; HRMS (ESI) Calcd for $C_{31}H_{23}N_2O$ [M^+ + H] m/z 439.1811, found 439.1808.

Compound ***30***. Yield 0.128 g (73%, white solid): mp 276−280 °C; IR (KBr, cm^{-1}) 3052, 2920, 1654, 1610, 1490, 1440, 1320, 1029, 821, 783, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94−8.93 (m, 1H), 8.48 (d, J = 8.0 Hz, 1H), 8.06−8.04 (m, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.50−7.48 (m, 1H), 7.39−7.35 (m, 3H), 7.24 (br s, 2H), 7.18−7.16 (m, 3H), 7.08 (s, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.83 (t, J ∼ 7.4 Hz, 1H), 6.75−6.70 (m, 2H), 6.49 (t, J = 7.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.8, 144.8, 143.1, 142.0, 138.3, 137.9, 136.8, 136.0, 135.1, 131.9, 131.8, 130.9, 130.8, 129.9, 128.8, 128.5, 128.3, 128.0, 127.8, 127.2, 126.7, 126.6, 126.4, 125.8, 125.4, 123.5, 121.5, 118.4, 22.1; HRMS (ESI) Calcd for $C_{31}H_{23}N_2O$ [M^+ + H] 439.1811, found 439.1810.

Compound ***31***. Yield 0.121 g (64%, white solid): mp 234−238 °C; IR (KBr, cm^{-1}) 3052, 2926, 1649, 1578, 1534, 1490, 1321, 1156, 1123, 833, 805, 740, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (d, J = 8.0 Hz, 1H), 8.93 (dd, J = 4.4 and 1.6 Hz, 1H), 8.07 (d, J = 8.8 Hz, 1H), 7.97 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.71−7.66 (m, 2H), 7.62−7.59 (m, 2H), 7.45−7.36 (m, 3H), 7.28−7.20 (m, 5H), 7.02 (d, J = 7.6 Hz, 1H), 6.86 (t, J ∼ 7.4 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H), 6.75 (t, J ∼ 7.6 Hz, 1H), 6.52 (t, J ∼ 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 150.9, 144.8, 143.6, 139.7, 138.4, 137.2, 136.1, 135.0, 133.8, 132.4, 132.3, 132.1, 132.0, 130.9, 130.7, 129.6, 128.9, 128.6, 128.4, 128.1$_4$, 128.1$_0$, 128.0, 127.3, 126.9, 126.7, 126.5, 126.4, 125.9, 123.8, 121.6, 119.0; HRMS (ESI) Calcd for $C_{34}H_{23}N_2O$ [M^+ + H] m/z 475.1811, found 475.1810.

Compound ***32***. Yield 0.173 g (64%, white solid): mp 278−282 °C; IR (KBr, cm^{-1}) 3057, 2942, 1649, 1594, 1479, 1408, 1331, 1260, 1090, 783, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 2.8 Hz, 1H), 8.59 (d, J = 7.6 Hz, 1H), 8.47−8.45 (m, 1H), 7.60 (t, J ∼ 7.2 Hz, 1H), 7.52 (t, J ∼ 7.4 Hz, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.34 (dd, J = 8.4 and 4.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.24 (br s, 2H), 7.17 (br s, 3H), 6.98 (d, J = 7.2 Hz, 1H), 6.85 (t, J ∼ 7.4 Hz, 1H), 6.80 (d, J = 7.6 Hz, 1H), 6.75 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.53 (t, J = 7.6 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 155.1, 151.0, 145.2, 142.4, 138.2, 136.8, 135.2, 132.4, 131.9, 131.7, 130.8$_4$, 130.7$_7$, 130.3, 129.9, 128.5, 128.0, 127.8, 127.2, 126.7, 126.6$_3$, 126.5$_8$, 126.5, 125.6, 121.1, 120.5, 118.4, 103.4, 55.8; HRMS (ESI) Calcd for $C_{31}H_{23}N_2O_2$[M^+ + H] 455.1760, found 455.1757.

Compound ***33***. Yield 0.089 g (51%, white solid): mp 212−216 °C; IR (KBr, cm^{-1}) 3052, 1644, 1556, 1523, 1496, 1326, 1271, 1030, 915, 811, 778, 712; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95−8.94 (m, 1H), 8.08−8.06 (m, 1H), 7.71−7.67 (m, 2H), 7.50 (d, J = 7.2 Hz, 1H), 7.40−7.37 (m, 2H), 7.24−7.16 (m, 5H), 7.05 (d, J = 5.2 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.85 (t, J = 7.6 Hz, 1H), 6.79−6.75 (m, 2H), 6.53 (t, J ∼ 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 150.9, 146.8, 144.8, 143.1, 137.3, 137.0, 136.1, 134.5, 133.3, 131.0$_4$, 130.9$_9$, 130.1, 129.4, 128.8, 127.9, 127.5, 126.8, 126.6, 125.8, 125.2, 121.6, 117.5; HRMS (ESI) Calcd for $C_{28}H_{19}N_2OS$ [M^+ + H] 431.1219, found 431.1217.

Compound ***34***. Yield 0.106 g (62%, white solid): mp 258−262 °C; IR (KBr, cm^{-1}) 3063, 1655, 1562, 1490, 1441, 1326, 1238, 1085, 1025, 860, 822, 712; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (dd, J = 4.0 and 1.6 Hz), 8.07 (dd, J = 4.4 and 1.6 Hz, 1H), 7.80 (d, J = 5.2 Hz, 1H), 7.69−7.67 (m, 1H), 7.50−7.48 (m, 1H), 7.40−7.36 (m, 2H), 7.32−7.28 (m, 3H), 7.23−7.12 (m, 3H), 6.98 (d, J = 8.0 Hz, 1H), 6.86 (t, J ∼ 7.4 Hz, 1H), 6.80−6.77 (m, 2H), 6.54 (t, J ∼ 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 151.4, 150.9, 144.8, 141.9, 137.5, 137.0, 136.1, 134.3, 130.9, 130.4, 130.0, 129.7, 128.8, 128.2, 127.6, 127.4, 126.9, 126.7, 126.2, 125.8, 124.9, 121.6, 116.5; HRMS (ESI) Calcd for $C_{28}H_{19}N_2OS$ [M^+ + H] 431.1219, found 431.1218.

Compound ***35***. Yield 0.092 g (56%, white solid): mp 252−256 °C; IR (KBr, cm^{-1}) 3057, 2986, 1676, 1588, 1539, 1490, 1364, 1282, 1073, 788, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94−8.93 (m, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 2.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.40−7.36 (m, 2H), 7.17 (br s, 5H), 6.95 (d, J = 7.6 Hz, 1H), 6.86 (t, J ∼ 7.4 Hz, 1H), 6.81−6.74 (m, 2H), 6.62 (d, J = 1.6 Hz, 1H), 6.54 (t, J ∼ 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 150.9, 148.4, 144.8, 142.6, 142.4, 137.1, 136.3, 136.1, 134.7, 134.5, 131.2, 130.5, 130.3, 128.9, 128.8, 128.0, 127.6, 126.9, 126.8, 126.6, 125.8, 121.6, 114.7, 107.9; HRMS (ESI) Calcd for $C_{28}H_{19}N_2O_2$ [M^+ + H] 415.1447, found 415.1445.

Compound ***36***. Yield 0.116 g (61%, white solid): mp 264−268 °C; IR [KBr (for crystals) cm^{-1}] 3036, 1655, 1468, 1321, 1068, 1030, 822, 751, 707 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (dd, J ∼ 4.2 Hz and ∼1.4 Hz, 1H), 8.07 (dd, J ∼ 4.2 Hz and ∼1.4 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.58−7.56 (m, 1H), 7.49−7.37 (m, 5H), 7.32−7.28 (m, 2H), 7.25−7.22 (m, 2H), 7.02 (d, J = 7.6 Hz, 1H), 6.95 (t, J ∼ 7.4 Hz, 1H), 6.85 (t, J ∼ 7.4 Hz, 1H), 6.82−6.78 (m, 2H), 6.74 (t, J ∼ 7.4 Hz, 1H), 6.51 (t, J = 7.6 Hz, 1H), 4.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 151.0, 145.0, 141.5, 138.2, 137.9, 137.3, 136.1, 134.8, 131.5, 131.2$_2$, 131.1$_7$, 131.1, 130.4, 128.8, 128.6, 128.2, 128.0, 127.1, 126.6, 126.5, 126.4, 126.2, 125.8, 124.9, 123.1, 122.1, 121.6, 119.8, 117.2, 109.9, 31.5; HRMS (ESI) Calcd for $C_{33}H_{24}N_3O$ [M^+ + H] 478.1920, found 478.1919. The compound crystallized as CH_3CN solvate (IR, ^{1}H NMR).

Compound ***37***. Isomer ratio 7:3; Yield 0.091 g (61%, gummy liquid); IR (neat, cm^{-1}) 2921, 1660, 1611, 1496, 1332, 1227, 800, 762; ^{1}H NMR (400 MHz, $CDCl_3$) for major isomer δ 8.90−8.89 (m, 1H), 8.49−8.45 (m, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.98−7.96 (m, 1H), 7.77−7.68 (m, 5H), 7.48−7.43 (m, 3H), 2.55−2.48 (m, 1H), 2.39 (s, 3H), 2.03−1.97 (m, 1H), 1.67−1.61 (m, 1H), 1.48 (br s, 1H), 1.36−1.35 (m, 4H), 1.05−1.00 (m, 2H), 0.72 (t, J ∼ 7.0 Hz, 3H); ^{13}C NMR for major isomer (100 MHz, $CDCl_3$) δ 163.3, 151.4, 144.9, 140.9, 138.4, 138.0, 137.6, 136.4, 132.5, 130.3, 130.1, 129.8, 129.5, 129.4, 129.1, 128.8, 128.5, 128.0, 126.5, 126.3, 125.8, 125.6, 125.5, 125.2, 122.8, 121.9, 113.9, 108.7, 31.0, 30.9, 29.0, 28.8, 22.3, 13.9, 13.7; HRMS (ESI) Calcd for $C_{25}H_{27}N_2O$ [M^+ + H] m/z 371.2124, found 371.2124. Many peaks for the minor isomer in the ^{1}H and ^{13}C NMR spectra were buried in those due to the major isomer (see Supporting Information, Figures S75−S76).

(iii). Synthesis of RuCl(OAc)(*p*-cymene) (38). To a solution of [{$RuCl_2$(*p*-cymene)}$_2$] (0.200g, 0.33 mmol) in *t*AmOH (35 mL), $Cu(OAc)_2{\cdot}H_2O$ (2.64g, 13.2 mmol) was added. The mixture was heated under reflux for 24 h. The resulting suspension was filtered through Celite to give a clear orange solution from which solvent was removed to get RuCl(OAc)(*p*-cymene) as an orange solid in 64% yield (0.137g). The spectroscopic data and melting point matched with the literature data.[18]

(iv). Preparation of Complex 40. This compound could be prepared by two slightly different methods.

A mixture of the amide **1a** (0.020g, 0.08 mmol) and **38** (0.026g, 0.08 mmol) was heated under reflux in *t*AmOH (5 mL) for 24 h. The resulting suspension was passed through a Celite pad, washed with DCM (10 mL) and concentrated in vacuo to give the complex **40** in quantitative yield.

A mixture of [{$RuCl_2$(*p*-cymene)}$_2$] (0.122g, 0.2 mmol), *N*-quinolin-8-yl-benzamide **1a** (0.050g, 0.2 mmol) and NaOAc (0.033g, 0.4 mmol) was taken in MeOH (8 mL) and heated under reflux for 2 h at 70 °C. The reaction mixture was concentrated in vacuo, and the product was purified by column chromatography on silica gel using EtOAc as eluent to afford the ruthenium complex **40**. It was crystallized from dichloromethane−hexane (1:1) mixture.

Compound ***40***. Yield 0.084 g (81%, orange crystals): mp 226−230 °C; IR (KBr, cm^{-1}) 3074, 2964, 1594, 1561, 1506, 1380, 1238, 1139, 1073, 925, 832, 723; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (d, J = 4.0 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.15−8.13 (m, 3H), 7.42−7.40 (m, 5H), 7.16 (d, J = 7.6 Hz, 1H), 5.56 (d, J = 5.6 Hz, 1H), 5.23 (d, J = 6.8 Hz, 1H), 5.11 (d, J = 5.6 Hz, 1H), 3.96 (d, J = 4.8 Hz, 1H), 2.32 (t, J = 7.4 Hz, 1H), 2.13 (s, 3H), 0.95 (d, J = 6.8 Hz, 3H), 0.84 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5, 151.0, 150.9, 145.3, 142.5, 137.8, 129.8, 129.5, 129.3, 127.7, 122.9, 121.6, 117.1, 105.2, 97.9, 86.2, 85.9, 82.2, 80.6, 30.8, 22.5, 21.9, 19.1; HRMS (ESI) Calcd for $C_{26}H_{25}ClN_2ORuNa$ [M^+ + Na] 541.0597, found 541.0602.

(v). Synthesis of Isoquinolone 3 Using Ruthenium Complex 40. A mixture of **40** (40 mg, 0.08 mmol), diphenylacetylene (27 mg, 0.15 mmol) and $Cu(OAc)_2·H_2O$ (30 mg, 0.15 mmol), and *t*AmOH (1 mL) was taken in a Schlenk tube. The resulting solution was heated on an oil bath at 110 °C for 24 h. The reaction mixture was filtered through a plug of Celite using EtOAc (30 mL) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using hexane:EtOAc (1:1) to afford the isoquinolone **3** (28 mg, 85%).

(vi). X-ray Data. X-ray data for compounds **3**, **13**, **16**, **17**, and **40** were collected using Mo Kα (λ = 0.710 73 Å) radiation. The structures were solved and refined by standard methods.[19] The CCDC numbers are CCDC 984683−984687.

3: $C_{30}H_{20}N_2O$, M = 424.48, Triclinic, space group $P\bar{1}$, a = 10.4838(12), b = 14.518(2), c = 15.9147(18) Å, V = 2196.2(5) Å^3, α = 79.164(11), β = 73.907(10), γ = 71.712(11), Z = 4, μ = 0.078 mm^{-1}. Data/restraints/parameters: 7726/2/595. R indices ($I > 2\sigma(I)$): $R1$ = 0.0596, $wR2$ (all data) = 0.1313. CCDC No. 984683.

13: $C_{22}H_{20}N_2O$, M = 328.40, Monoclinic, space group $P2(1)/c$, a = 13.1006(16), b = 14.6841(17), c = 8.7923(8).Å, β = 100.348(9), V = 1663.9(3) Å^3, Z = 4, μ = 0.081 mm^{-1}. Data/restraints/parameters: 2941/0/228. R indices ($I > 2\sigma(I)$): $R1$ = 0.0464, $wR2$ (all data) = 0.1201. CCDC No. 984684.

16: $C_{25}H_{18}N_2O$, M = 362.41, Triclinic, space group $P\bar{1}$, a = 7.4501(15), b = 8.7551(18), c = 14.931(3) Å, α = 95.20(3), β = 98.89(3), γ = 103.19(3), V = 928.8(3) Å^3, Z = 2, μ = 0.080 mm^{-1}. Data/restraints/parameters: 3613/0/254. R indices ($I > 2\sigma(I)$): $R1$ = 0.0494, $wR2$ (all data) = 0.1434. CCDC No. 984685.

17: $C_{31}H_{21}N_3O_3$, M = 483.51, Monoclinic, space group $P2(1)/n$, a = 9.5537(15), b = 16.927(3), c = 15.612(3) Å, β = 105.520(3), V = 2432.6(7) Å^3, Z = 4, μ = 0.086 mm^{-1}. Data/restraints/parameters: 4266/0/335. R indices ($I > 2\sigma(I)$): $R1$ = 0.0736, $wR2$ (all data) = 0.2303. CCDC No. 984686.

40: $C_{26}H_{25}ClN_2ORu$, M = 518.00, Orthorhombic, space group $P2(1)2(1)2(1)$, a = 7.8508(2), b = 15.8682(4), c = 18.2984(4) Å, V = 2279.57(10) Å^3, Z = 4, μ = 6.798 mm^{-1}. Data/restraints/parameters: 3629/0/283. Flack parameter 0.49(1). R indices ($I > 2\sigma(I)$): $R1$ = 0.0340, $wR2$ (all data) = 0.0915. CCDC No. 984687.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures and CIF files giving ORTEP drawings as shown by X-ray crystallography, and copies of ^{1}H and ^{13}C NMR spectra of all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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