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# Synthesis of Azaheterocycles from Aryl Ketone *O*-Acetyl Oximes and Internal Alkynes by Cu−Rh Bimetallic Relay Catalysts

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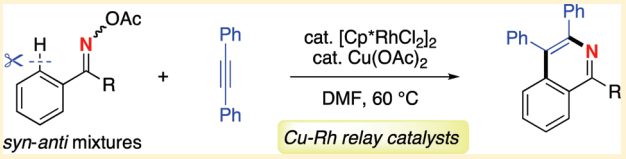
Supporting Information

**ABSTRACT:** A synthetic method for azaheterocycles from aryl ketone *O*-acetyl oximes and internal alkynes has been developed by using the $Cu(OAc)_2$−$[Cp^*RhCl_2]_2$ bimetallic catalytic system. The reactions proceeded with both of *anti*- and *syn*-isomers of oximes with a wide scope of substituents. The Cu−Rh bimetallic system could be applied for the synthesis of isoquinolines as well as *β*-carboline, furo[2.3-*c*]pyridine, pyrrolo[2,3-*c*]pyridine, and thieno[2,3-*c*]pyridine derivatives.

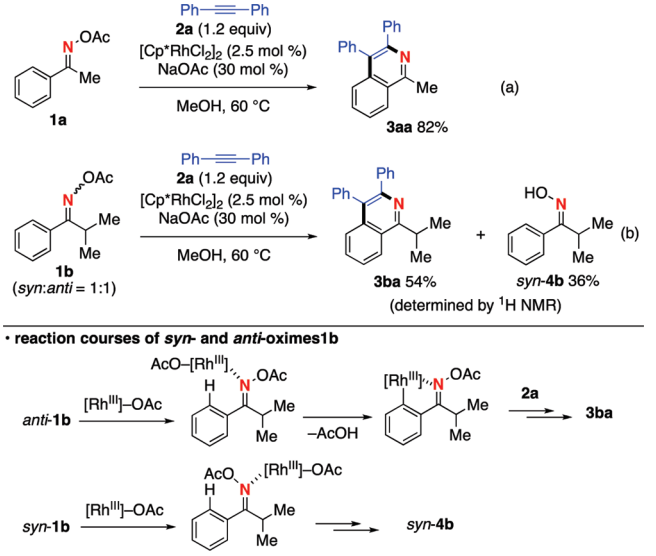



## INTRODUCTION

Nitrogen-containing heterocyclic compounds (azaheterocycles) are one of the most prevalent components in numerous natural products, potent pharmaceutical drugs, and various kinds of functional materials. Although diverse synthetic methodologies toward azaheterocycles have been developed,[1] versatile and flexible approaches to construct azaheterocycles with selective control of substitution patterns using readily available building blocks are still needed.

Chemical transformation via catalytic C−H bond activation by various transition metal complexes is a powerful tool in organic synthesis.[2] In the process of the C−H functionalization, suitable heteroatoms in the substrates are commonly utilized to direct a metal complex to the specific proximal C−H bond. Among such directing groups, an $sp^2$ nitrogen atom of the imine derivatives has played a crucial role in numerous examples of C−H bond activation with the rational catalyst design,[3] while these nitrogen atoms have rarely been involved for a new bond constructed in reaction processes.[4] The Davies group revealed that the combined use of $[Cp^*RhCl_2]_2$ and NaOAc generates $Cp^*Rh(OAc)_n$ species and results in fission of certain C−H bonds with the aid of an intramolecular directing group such as the imino group to afford rhodacycle complexes.[5] This chemistry has been deeply investigated by the Jones group in terms of the reactivity of the rhodacycles as well as the reaction mechanism of the cyclometalation.[6] Recently, this method has been successfully applied to various kinds of oxidative heterocycle syntheses with insertion of alkynes.[2b,7] For example, Fagnou and Miura-Satoh have independently reported the Rh(III)-catalyzed oxidative isoquinoline synthesis using *N*-*t*-Bu aryl aldimines[7h] and benzophenone *N*-H imines,[7i] respectively, as a nitrogen containing source via *o*-aryl C−H rhodation followed by internal alkyne insertion and C−N reductive elimination, where a stoichiometric use of $Cu(OAc)_2$ as an external oxidant is indispensable to regenerate the active Rh(III) catalyst. On the basis of this background, to achieve the entire catalytic process for synthesis of isoquinoline derivatives under milder reaction conditions, our attention has been drawn to the potential chemical reactivity of readily available aryl ketoxime derivatives. This is a full account on the synthesis of azaheterocycles from aryl ketone *O*-acetyl oximes with internal alkynes using a copper−rhodium bimetallic catalytic system, where both *anti*- and *syn*-isomers of oximes could be utilized with a wide scope of substituents.

**Scheme 1. Synthesis of Isoquinolines Catalyzed by $[Cp^*RhCl_2]_2$−NaOAc**

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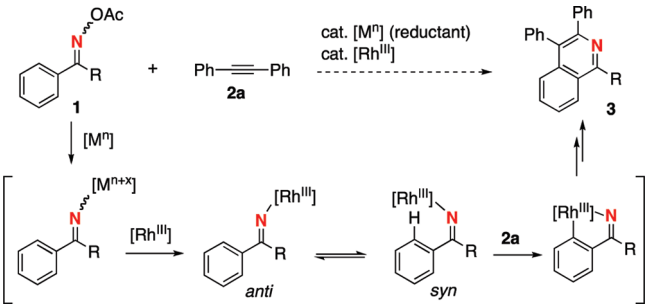
## RESULTS AND DISCUSSION

Recently, elegant strategies using the N−O bond in the directing group as an internal oxidant have emerged for *ortho* C−H activation and C−N bond formation. The reactions are redox-neutral, and stoichiometric external oxidants are not required.[8,9] For example, Guimond disclosed Rh(III)-catalyzed redox-neutral synthesis of isoquinolones from benzhydroxamic acid derivatives and alkynes.[9a] Our group also reported a preliminary result of isoquinoline formation utilizing aryl ketone *anti*-*O*-acetyl oximes with internal alkynes under the catalytic redox-neutral $[Cp^*RhCl_2]_2$−NaOAc system (Scheme 1),[9b,10] whereas a stereochemical requirement of oximes **1** (i.e., the N−O bond of oximes should be *anti* to the aryl moiety) should be a hurdle of the process especially in the case of the substrates bearing a bulky substituent such as isobutyrophenone *O*-acetyl oxime (*syn*:*anti* = 1:1). Actually, the reaction of oxime **1b** and diphenylacetylene (**2a**) with 2.5 mol % of $[Cp^*RhCl_2]_2$ and 30 mol % of NaOAc as an acetate source in MeOH (0.2 M) at 60 °C provided the desired isoquinoline **3ba** in a modest 54% yield with recovery of *syn*-isobutyrophenone oxime in 36% yield through deacetylation (Scheme 1b). This drawback could be attributed to the reaction mechanism of C−H rhodation, where the rhodium center should be directed to the *ortho* C−H bond of aryl ketone *O*-acetyl oximes **1** with the aid of the lone pair of the oxime $sp^2$ nitrogen for *ortho* C−H rhodation prior to the N−O bond cleavage/C−N bond formation.

To solve this problem, we planned to utilize the reduction of the oxime N−O bond as an initiation of the process by using lower valent transition metals $[M^n]$ such as Pd(0)[11] and Cu(I)[12,13] complexes to generate the corresponding iminyl metal species (Scheme 2). If such a metal reductant of oximes and the Rh(III) complex could work independently in the same reaction system, the resulting iminyl metals might then undergo transmetalation with Rh(III) to give iminyl rhodium(III) intermediates, which could successively achieve *ortho* C−H rhodation and annulation with alkynes. As iminyl metal species should be free to isomerize between *anti*- and *syn*-isomers,[14,15] both of the isomers could be utilized in this transformation.

Based on our working hypothesis as shown in Scheme 2, our studies commenced with the reaction of isobutyrophenone *O*-acetyl oxime (*syn*:*anti* = 1:1) (**1b**) and diphenylacetylene (**2a**) (1.2 equiv) by the use of $[Cp^*RhCl_2]_2$ combined with metal reductants such as Pd(0) and Cu(I) complexes (Table 1). In the cases of Pd(0) complexes as a reductant with combined use of NaOAc (entries 1 and 2), the reactions resulted in a complex mixture including only a small amount of isoquinoline **3ba**. On the contrary, the reaction in the presence of 10 mol % of $Cu^IOAc$ in DMF under a nitrogen atmosphere proceeded smoothly to

**Scheme 2. Working Hypothesis**




**Scheme 3. Proposed Reaction Pathway**

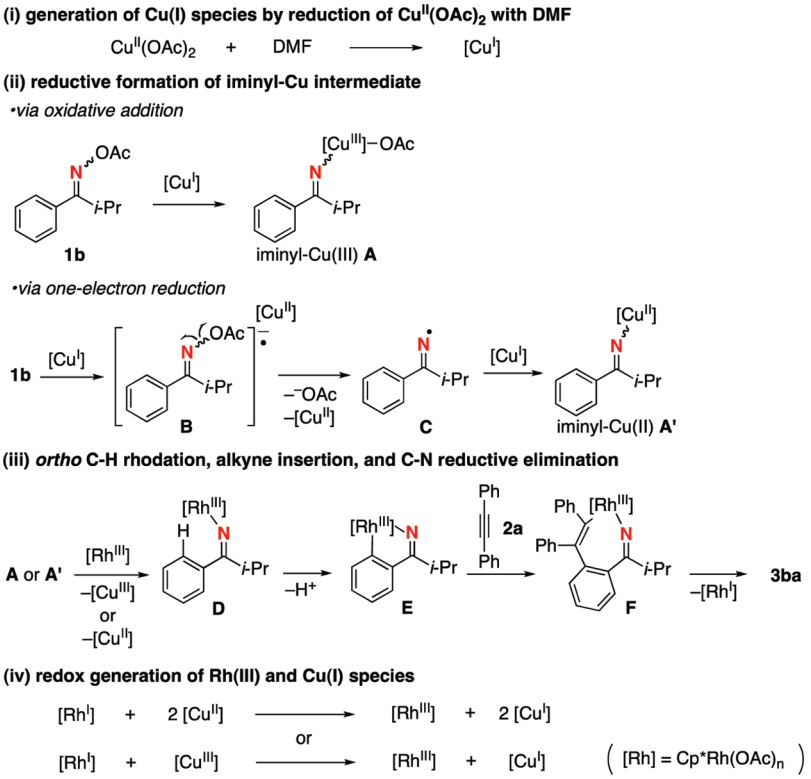




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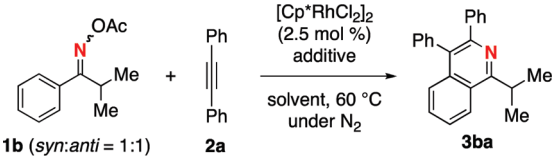
**Table 1. Optimization of Reaction Conditions for Pyridine Formation**[a]




| entry | additive (mol %) | solvent | time | yield (%) of **3ba**[b] |
|---|---|---|---|---|
| 1 | $Pd(dba)_2$ (20) + NaOAc (30) | DMF | 15 h | 14[c] |
| 2 | $Pd(PPh_3)_4$ (20) + NaOAc (30) | DMF | 15 h | 19[c] |
| 3 | CuOAc (10) | DMF | 45 min | 99 |
| 4 | $Cu(OAc)_2$ (10) | DMF | 4 h | 95 |
| 5[d] | $Cu(OAc)_2$ (10) | DMF | 24 h | 20[e] |
| 5 | $Cu(OAc)_2$ (10) | MeOH | 1 h | 80[f] |
| 6 | $Cu(OAc)_2$ (10) | toluene | 22 h | 0[g] |

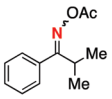
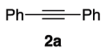
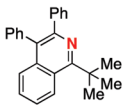
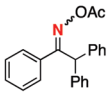
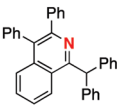
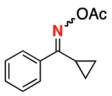
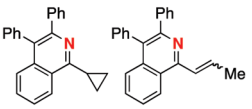
[a] The reactions were carried out by treatment of a mixture of oxime **1b** (0.3 mmol) and alkyne **2a** (1.2 equiv) with $[Cp^*RhCl_2]_2$ (2.5 mol %) and $Cu(OAc)_2$ (10 mol %) at 60 °C under $N_2$ atmosphere. [b] Isolated yields. [c] The reaction resulted in a complex mixture. [d] The reaction was run under an air atmosphere. [e] Oxime **1b** was recovered in 40% yield. [f] Deacetylated oxime was formed in 15% yield. [g] **1b** was recovered in 51% yield.

give isoquinoline **3ba** in quantitative yield within 45 min, where both *syn*- and *anti*-isomers of **1a** were reacted (entry 3). It was noteworthy that utilization of $Cu^{II}(OAc)_2$ instead of $Cu^{I}OAc$ provided **3ba** in comparable yield, although a longer reaction time (4 h) was required (entry 4). In this case, Cu(I) species might be generated *in situ* via reduction of $Cu^{II}(OAc)_2$ by DMF,[16,17] which could be supported by observation of the sluggish reaction under an air atmosphere (entry 5). Instead of DMF as a solvent, MeOH could be utilized with $Cu(OAc)_2$, while deacetylation competed along with the isoquinoline formation (entry 5). No isoquinoline **3ba** was formed in the reaction with $Cu^{II}(OAc)_2$ without $[Cp^*RhCl_2]_2$, which indicated that synergistic Cu−Rh cooperation should be indispensable for the present isoquinoline formation from a *syn*,*anti* mixture of *O*-acetyl oxime **1b**.

A proposed mechanism for the $Cu(OAc)_2$−$[Cp^*RhCl_2]_2$ bimetallic catalytic system is outlined in Scheme 3. First, $Cu^{II}(OAc)_2$ might be reduced by DMF to form Cu(I) species (step i). Two pathways are proposed for the generation of iminyl copper species (step ii). Oxidative addition of the N−O bond of *O*-acetyl oximes could directly generate iminyl copper(III) **A**. Alternatively, one electron reduction of *O*-acetyl oximes by Cu(I) species could form anion radical **B**. The homolytic N−O bond cleavage of **B** might afford putative iminyl radical **C**, which could be further reduced by another Cu(I) to give iminyl copper(II) **A′**.[18] Formation of rhodacycle **E** from iminyl copper species **A** or **A′** with Rh(III) via iminyl rhodium **D**, subsequent insertion of alkyne **2a**, and C−N reductive elimination from **F** provided isoquinoline **3ba** with generation of Rh(I) species (step iii). Finally, redox reactions between Rh(I) and Cu(II) or Cu(III) species would lead to regeneration of Rh(III) and Cu(I) (step iv).

By using the optimized $Cu(OAc)_2$-$[Cp^*RhCl_2]_2$ catalytic system,[19] the generality for the synthesis of isoquinolines was next examined (Table 2). An examination of the scope of alkynes revealed that both methoxy and bromo-substituted diarylacetylenes

**Table 2. Synthesis of Isoquinolines from Aryl Ketone *O*-Acetyl Oximes and Internal Alkynes**[a]

| entry | oxime **1** (*syn* : *anti*) | alkyne **2** | product **3** / yield[b] |
|---|---|---|---|
| |  |  |  |
| 1 | **1b** (1:1) | **2b** ($R^1$, $R^2$ = 4-MeO-$C_6H_4$) | **3bb** 87% |
| 2 | **1b** (1:1) | **2c** ($R^1$, $R^2$ = 4-Br-$C_6H_4$) | **3bc** 92% |
| 3 | **1b** (1:1) | **2d** ($R^1$, $R^2$ = *n*-Pr) | **3bd** 78% |
| 4 | **1b** (1:1) | **2e** ($R^1$, $R^2$ = $CH_2OTBS$) | **3be** 79% |
| 5 | **1b** (1:1) | **2f** ($R^1$ = Me, $R^2$ = Ph) | **3bf** 93% |
| 6 | **1b** (1:1) | **2g** ($R^1$ = $CH_2OTBS$, $R^2$ = Ph) | **3bg** 98% (13:1)[c],[d] |
| 7 | **1b** (1:1) | **2h** ($R^1$ = $CO_2Et$, $R^2$ = Ph) | **3bh** 75% (1.7:1)[e] |
| 8 | **1b** (1:1) | **2i** ($R^1$ = *n*-hexyl, $R^2$ = 2-thienyl) | **3bi** 81% |
| 9 |  **1c** (*syn*) |  **2a** |  **3ca** 99% |
| 10 |  **1d** (*syn*:*anti* = 2:1) | **2a** |  **3da** 78%[e] |
| 11 |  **1e** (*syn*:*anti* = 1:2.2) | **2a** |  **3ea**, 57% **3ea′**, 30% (*E*:*Z* = 6.5:1) |

[a] The reactions were carried out by treatment of a mixture of oxime **1** (0.5 mmol) and alkyne **2** (1.2 equiv) with $[Cp^*RhCl_2]_2$ (2.5 mol %) and $Cu(OAc)_2$ (10 mol %) in DMF (0.2 M) at 60 °C for 4−10 h under $N_2$ atmosphere. [b] Isolated yield. [c] Isolated as a mixture of regioisomers. [d] Regioselectivity was determined by NOESY experiments. [e] The reaction was conducted for 22 h.

**2b** and **2c** as well as dialkylacetylenes **2d** and **2e** reacted smoothly with isobutyrophenone *O*-acetyl oxime (**1b**) to afford isoquinolines **3** in good yields (entries 1−4). Insertion of unsymmetrical alkynes occurred with high regioselectivity except for that of ethyl 3-phenylpropiolate (**2h**) (entries 5−8). The reaction of *tert*-butyl ketone *O*-acetyl oxime (**1c**), which is a pure *syn*-isomer, afforded the corresponding isoquinoline **3ca** in excellent yield (entry 9). In the case of the reaction of 1,2,2-triphenylethanone *O*-acetyl oxime (**1d**), isoquinoline **3da** was formed selectively in 78% yield (entry 10), while Hartwig reported that the Pd(0) complex catalyzed intramolecular C−H amination to form indoles from this kind of oxime.[11a] When cyclopropyl ketone *O*-acetyl oxime **1e** (*syn*:*anti* = 1:2.2) was treated with diphenylacetylene (**2a**) under the present reaction conditions, cyclopropyl isoquinoline **3ea** was formed in 57% yield along with unexpected alkenyl isoquinoline **3ea′** in 30% yield as an *E*,*Z*-mixture (*E*:*Z* = 6.5:1) (entry 11).[20]

To probe the further potential of this Cu−Rh bimetallic system, we examined the reaction of indolyl ketoxime **5a** (the *anti*-isomer) with diphenylacetylene (**2a**) (1.5 equiv) (Table 3, entry 1). The reaction under the $Cu(OAc)_2$-$[Cp^*RhCl_2]_2$ catalytic system afforded *β*-carboline **6aa** in 82% yield, whereas the previous catalytic conditions with $[Cp^*RhCl_2]_2$−NaOAc gave **6aa** only in 42% yield along with isolation of deacetylated oxime **7a** in 25% yield. This result prompted us to further examine the scope and limitation of heteroaryl ketone *O*-acetyl oxime derivatives and alkynes for synthesis of *β*-carbolines and


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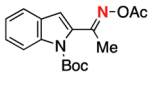
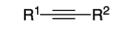
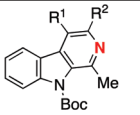
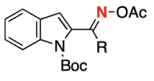
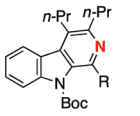
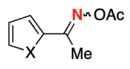
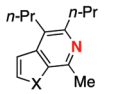
**Table 3. Reactions of Heteroaryl Ketone *O*-Acetyl Oxime Derivatives**[a]

| entry | oxime **5** (*syn* : *anti*) | alkyne **2** | product **5** / yield[b] |
|---|---|---|---|
| |  |  |  |
| 1 | **5a** (*anti*) | **2a** ($R^1 = R^2$ = Ph) | **6aa** 82% (42%)[c] |
| 2 | **5a** (*anti*) | **2b** ($R^1 = R^2$ = 4-MeO-$C_6H_4$) | **6ab** 28%[d] |
| 3 | **5a** (*anti*) | **2c** ($R^1 = R^2$ = 4-Br-$C_6H_4$) | **6ac** 69%[d] |
| 4 | **5a** (*anti*) | **2d** ($R^1 = R^2$ = *n*-Pr) | **6ad** 87% |
| 5 | **5a** (*anti*) | **2f** ($R^1$ = Me, $R^2$ = Ph) | **6af** 65% (5:1)[e] |
| 6 | **5a** (*anti*) | **2g** ($R^1$ = $CH_2OTBS$, $R^2$ = Ph) | **6ag** 50% (3:1)[e] |
| 7 | **5a** (*anti*) | **2j** ($R^1$ = $CO_2Me$, $R^2$ = Ph) | **6aj** 71% (1:1)[e] |
| |  |  |  |
| 8 | **5b** (R = *n*-Bu, *anti*) | **2d** | **6bd** 91% |
| 9 | **5c** (R = $CH_2CH_2CH{=}CH_2$, *anti*) | **2d** | **6cd** 36%[d],[f] |
| 10 | **5d** (R = $CO_2Et$, *anti*) | **2d** | **6dd** 60%[d] |
| 11 | **5e** (R = H, *anti*) | **2d** | **6ed** 40%[d],[g] |
| 12 |  **5f** (*anti*) | **2d** |  **6fd** 86% |
| |  | |  |
| 13 | **5g** (X = NTs, *anti*) | **2d** | **6gd** 91% |
| 14 | **5h** (X = O, *syn*:*anti* = 1:20) | **2d** | **6hd** 77% |
| 15 | **5i** (X = S, *syn*:*anti* = 1:4) | **2d** | **6id** 81% |

[a] The reactions were carried out by treatment of a mixture of oxime **5** (0.5 mmol) and alkyne **2** (1.5 equiv) with $[Cp^*RhCl_2]_2$ (2.5 mol %) and $Cu(OAc)_2$ (30 mol %) in DMF (0.2 M) at 60 °C for 2−9 h under $N_2$ atmosphere. [b] Isolated yield. [c] The yield under $[Cp^*RhCl_2]_2$ (2.5 mol %) and NaOAc (30 mol %) in MeOH (0.2 M) at 60 °C; 25% yield of deacetylated oxime **7a** was isolated. [d] The reaction was conducted using 5 mol % of $[Cp^*RhCl_2]_2$. [e] Regioselectivity was determined by NOESY experiments. [f] Deacetylated product of oxime **5c** was observed in 16% yield. [g] The reaction was conducted for 24 h, and *tert*-butyl 2-cyano-1*H*-indole-1-carboxylate (**8**) was obtained in 51% yield.

their derivatives under the $Cu(OAc)_2$-$[Cp^*RhCl_2]_2$ catalytic conditions. Di(4-bromophenyl)acetylene (**2c**) reacted smoothly with *O*-acetyl oxime **5a** to provide $\beta$-carboline **6ac** in 69% yield, while di(4-methoxyphenyl)acetylene (**2b**) gave $\beta$-carboline **6ab** in a lower yield of 28% (entries 2 and 3). The reaction of 4-octyne (**2d**) proceeded smoothly (entry 4). Insertion of unsymmetrical alkynes **2f** and **2g** proceeded regioselectiviely albeit in lower selectivity (entries 5 and 6) than that of the isoquinoline formation (see Table 2). In the case of methyl 3-phenylpropiolate (**2j**), a 1:1 regioisomeric mixture of $\beta$-carboline **6aj** was formed (entry 7). The reaction of indolyl *O*-acetyl oxime **5b** bearing a linear alkyl chain affords corresponding carboline **6bd** in 91% yield (entry 8). Alkenyl and alkoxycarbonyl moieties on *O*-acetyl oxime **5** are also tolerated under the reaction condition albeit in moderate yield (entries 9 and 10). Indolyl carbaldehyde *O*-acetyl oxime (**5e**) reacted with 4-octyne (**2d**) to afford $\beta$-carboline **6ed** in 40% yield along with the formation of carbonitrile **8** in 51% yield (entry 11).[21] In addition to the indolyl ketoximes, benzofuranyl, furanyl, pyrrolyl, and thienyl ketoximes could be coupled with 4-octyne (**2d**), forming the corresponding azaheterocycles in good yields (entries 12−15).

## CONCLUSION

We have developed synthetic methods for isoquinoline derivatives from readily available aryl ketone *O*-acetyl oxime and internal alkynes by using $Cu(OAc)_2$−$[Cp^*RhCl_2]_2$ bimetallic relay catalysts. The catalytic system could be applied for both *anti*- and *syn*-isomers of oximes toward synthesis of a variety of isoquinolines derivatives. A proposed mechanism involves the synergistic Cu−Rh cooperation characterized by the following relay steps: (1) Cu(I)-mediated reductive formation of iminyl copper species from *O*-acetyl oximes; (2) formation of iminyl rhodium species by transmetalation, aryl C−H rhodation, alkyne insertion, and C−N bond reductive elimination to afford azaheterocycles. Further exploitation of the other types of multimetallic cooperation, which would achieve unprecedented organic transformations, is currently underway.

## EXPERIMENTAL SECTION

**General.** $^1$H NMR (400 MHz) spectra were recorded in $CDCl_3$ [using $(CH_3)_4Si$ (for $^1$H, $\delta$ = 0.00) as internal standard]. $^{13}$C NMR (100 MHz) spectra were recorded in $CDCl_3$ [using $CDCl_3$ (for $^{13}$C, $\delta$ = 77.00) as internal standard]. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Alkynes **2b**,[22] **2c**,[22] **2e**,[23] **2g**,[24] and **2i**[25] were prepared by following reported procedures.

**Preparation of Aryl Ketone *O*-Acetyl Oximes 1 and Benzofuranyl, Pyrrolyl, Furanyl, and Thienyl Ketone *O*-Acetyl Oximes 5f−i. Typical Procedure for Synthesis of Isobutyrophenone *O*-Acetyl Oxime (1b).** To a solution of isobutyrophenone (0.90 g, 6.07 mmol) and pyridine (1.4 mL, 9.2 mmol) in EtOH (6 mL) was added $NH_2OH\cdot HCl$ (0.64 g, 17.1 mmol) in one portion, and the reaction mixture was stirred at 60 °C for 2 h. The reaction was quenched by adding water, and the organic materials were extracted twice with ethyl acetate. The combined extracts were washed with 1 N aqueous HCl and brine and dried over $MgSO_4$. Volatile materials were removed in vacuo to give acetophenone oxime, which was used for the next acetylation without further purification. The crude residue of acetophenone oxime obtained above was treated with $Ac_2O$ (1.2 mL, 12.2 mmol) and a catalytic amount of DMAP (5 mg) in pyridine (3 mL), and the reaction mixture was stirred at room temperature for 1 h. After volatile materials were evaporated, the resulting residue was treated with water, and organic materials were extracted twice with ethyl acetate. The combined extracts were washed with 1 N aqueous HCl and brine and dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 80:20) to yield the product **1b** (1.21 g, 5.89 mmol) in 97% yield.

**Isobutyrophenone *O*-acetyl Oxime (1b).** Colorless oil; IR (NaCl) 2970, 2934, 1626, 1466, 1445, 1366, 1206 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.17 (6H × 1, d, $J$ = 6.8 Hz), 1.22 (6H × 1, d, $J$ = 7.2 Hz), 1.95 (3H × 1, s), 2.23 (3H × 1, s), 2.99 (1H × 1, septet, $J$ = 6.8 Hz), 3.53 (1H × 1, septet, $J$ = 7.2 Hz), 7.13−7.16 (2H × 1, m), 7.34−7.45 (3H × 1 + 5H × 1, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 19.49, 19.53, 19.77, 19.81, 29.9, 34.9, 126.7, 128.0, 128.1, 128.2, 128.7, 129.4, 132.9, 133.9, 168.79, 168.83, 171.6, 171.9. ESIHRMS: found $m/z$ 206.1189, calcd for $C_{12}H_{16}NO_2$ $(M + H)^+$ 206.1181.

**(*Z*)-2,2-Dimethylpropiophenone *O*-Acetyl Oxime (1c).** Prepared from 2,2-dimethylpropiophenone and purified by recrystallization from hexane/ethyl acetate (two times) (84% yield). White solid; mp 74−75 °C; IR (NaCl) 2974, 2934, 1753, 1622, 1479, 1443, 1366 cm$^{-1}$;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$^1$H NMR (400 M + Hz, $CDCl_3$) $\delta$ 1.24 (9H, s), 1.89 (3H, s), 7.01−7.04 (2H, m), 7.34−7.41 (3H, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 19.6, 28.0, 38.3, 126.6, 127.8, 128.1, 133.2, 168.9, 174.8. ESIHRMS: found $m/z$ 220.1340, calcd for $C_{13}H_{18}NO_2$ $(M + H)^+$ 220.1338.

**1,2,2-Triphenylethanone *O*-Acetyl Oxime (1d).** Prepared from 1,2,2-triphenylethanone[26] and purified by flash column chromatography (silica gel, hexane/ethyl acetate = 80:20) (65% yield). Colorless oil; IR (NaCl) 3061, 3026, 1769, 1599, 1495, 1366, 1200, 1001 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.86 (3H × 0.5, s), 1.98 (3H × 1, s), 5.44 (1H × 1, s), 6.01 (1H × 0.5, s), 7.03−7.05 (2H × 1, m), 7.19 (2H × 1, d, $J$ = 7.2 Hz), 7.24−7.34 (11H × 1 + 13H × 0.5, m), 7.48−7.52 (2H × 0.5, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 19.2, 19.7, 53.5, 57.9, 127.0, 127.2, 127.4, 128.0, 128.3, 128.4, 128.5, 128.6, 129.0, 129.2, 129.4, 130.0, 133.4, 134.9, 138.6, 138.7, 166.6, 167.6, 167.9, 169.1. ESIHRMS: found $m/z$ 330.1497, calcd for $C_{22}H_{20}NO_2$ $(M + H)^+$ 330.1494.

**Cyclopropyl(phenyl)methanone *O*-Acetyl Oxime (1e).** Prepared from cyclopropyl(phenyl)methanone and purified by flash column chromatography (silica gel, hexane/ethyl acetate = 80:20) (quantitative yield). Colorless oil; IR (NaCl) 3017, 1769, 1759, 1601, 1493, 1366, 1207 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.68−0.72 (2H × 1, m), 0.84−0.89 (2H × 0.45, m), 0.90−0.95 (2H × 0.45, m), 0.98−1.03 (2H × 1, m), 1.91−1.98 (1H × 0.45, m), 1.95 (3H × 0.45, s), 2.25 (3H × 1, s), 2.36−2.42 (1H × 1, m), 7.23−7.25 (2H × 0.45, m), 7.35−7.41 (5H × 1 + 3H × 0.45, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 6.3, 6.5, 10.7, 15.7, 19.5, 19.8, 127.1, 128.06, 128.08, 128.8, 129.1, 129.5, 131.8, 132.3, 168.6, 168.96, 169.01, 169.2. ESIHRMS: found $m/z$ 204.1026, calcd for $C_{12}H_{14}NO_2$ $(M + H)^+$ 204.1025.

**1-(Benzofuran-2-yl)ethanone *O*-Acetyl Oxime (5f).** Prepared from 1-(benzofuran-2-yl)ethanone and purified by recrystallization from hexane/ethyl acetate (one time) (68% yield). White solid; mp 101−102 °C; IR (NaCl) 1773, 1607, 1560, 1449, 1368, 1306 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.29 (3H, s), 2.42 (3H, s), 7.25−7.29 (2H, m), 7.38 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.56 (1H, dd, $J$ = 0.8, 8.4 Hz), 7.62 (1H, d, $J$ = 7.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 13.3, 19.6, 109.8, 112.0, 121.8, 123.4, 126.6, 127.5, 149.9, 154.3, 155.5, 168.2. ESIHRMS: found $m/z$ 218.0811, calcd for $C_{12}H_{12}NO_3$ $(M + H)^+$ 218.0817.

**(*E*)-1-(1-Tosyl-1*H*-pyrrol-2-yl)ethanone *O*-Acetyl Oxime (5g).** Prepared from 1-(1-tosyl-1H-pyrrol-2-yl)ethanone[27] and purified by recrystallization from hexane/ethyl acetate (two times) (68% yield). White solid; mp 113−115 °C; IR (NaCl) 1767, 1597, 1368, 1263, 1175, 1148 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.24 (3H, s), 2.38 (6H, s), 6.25 (1H, t, $J$ = 3.2 Hz), 6.40 (1H, dd, $J$ = 1.6, 3.2 Hz), 7.27 (1H, dd, $J$ = 1.6, 3.2 Hz), 7.28 (2H, d, $J$ = 8.4 Hz), 7.77 (2H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 19.2, 19.6, 21.6, 113.1, 117.9, 125.4, 127.5, 129.7, 129.8, 135.2, 145.3, 158.9, 168.1. ESIHRMS: found $m/z$ 321.0904, calcd for $C_{15}H_{17}N_2O_4S$ $(M + H)^+$ 321.0909.

**1-(Furan-2-yl)ethanone *O*-Acetyl Oxime (5h).** Prepared from 1-(furan-2-yl)ethanone and purified by recrystallization from hexane/ethyl acetate (two times) (70% yield). White solid; mp 99−100 °C; IR (NaCl) 1771, 1609, 1481, 1393, 1368, 1325 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.25 (3H × 1, s), 2.28 (3H × 0.05), 2.31 (3H × 1, s), 2.41 (3H × 0.05), 6.49 (1H × 1, dd, $J$ = 1.8, 3.6 Hz), 6.59 (1H × 0.05, dd, $J$ = 1.6, 3.6 Hz), 6.91 (1H × 1, dd, $J$ = 0.4, 3.6 Hz), 7.35 (1H × 0.05, dd, $J$ = 0.4, 3.6 Hz), 7.54 (1H × 1, dd, $J$ = 0.6, 1.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 13.1, 19.6, 111.7, 113.2, 145.0, 148.3, 153.8, 168.4. ESIHRMS: found $m/z$ 168.0656, calcd for $C_8H_{10}NO_3$ $(M + H)^+$ 168.0661.

**1-(Thiophen-2-yl)ethanone *O*-Acetyl Oxime (5i).** Prepared from 1-(thiophen-2-yl)ethanone and purified by recrystallization from hexane/ethyl acetate (two times) (85% yield). White solid; mp 115−117 °C; IR (NaCl) 1763, 1603, 1526, 1431, 1368, 1306, 968 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.26 (3H × 1, s), 2.33 (3H × 0.75, s), 2.40 (3H × 1, s), 2.51 (3H × 0.75, s), 7.07 (1H × 1, dd, $J$ = 4.0, 5.2 Hz), 7.16 (1H × 0.25, dd, $J$ = 3.6, 5.2 Hz), 7.42 (1H × 1, dd, $J$ = 1.0, 5.0 Hz), 7.44 (1H × 1, dd, $J$ = 1.0, 3.8 Hz), 7.58 (1H × 0.25, dd, $J$ = 1.2, 4.0 Hz), 7.67 (1H × 0.25, dd, $J$ = 1.2, 5.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 19.7, 19.92, 19.94, 126.2, 127.2, 129.0, 129.1, 131.7, 132.2, 132.7, 137.8, 153.3, 157.6, 167.6, 168.7. ESIHRMS: found $m/z$ 184.0435, calcd for $C_8H_{10}NO_2S$ $(M + H)^+$ 184.0432.

**Preparation of Indolyl Ketone *O*-Acetyl Oximes 5a−e. Typical Procedure for Synthesis of (*E*)-*tert*-Butyl 2-(1-(acetoxyimino)ethyl)-1*H*-indole-1-carboxylate (5a).** To a solution of 1-(1*H*-indol-2-yl)ethanone[28] (1.75 g, 11.0 mmol) in $CH_2Cl_2$ (27 mL) was added 4-(dimethylamino)pyridine (0.13 g, 1.1 mmol) and di-*tert*-butyl dicarbonate (2.62 g, 12.0 mmol). The reaction mixture was stirred at room temperature for 2.5 h, then quenched with 1 N aqueous HCl, and extracted thrice with $CH_2Cl_2$. The combined organic extracts were washed with water and brine and dried over anhydrous $MgSO_4$. Volatile materials were removed in vacuo, and *tert*-butyl 2-acetyl-1*H*-indole-1-carboxylate was used for the next step without purification. To a solution of *tert*-butyl 2-acetyl-1*H*-indole-1-carboxylate in EtOH (5 mL) were added pyridine (2.5 mL, 30.4 mmol) and $NH_2OH \cdot HCl$ (1.13 g, 16.4 mmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was then quenched with water and extracted twice with ethyl acetate. The combined organic extracts were washed with 1 N aqueous HCl and brine and dried over anhydrous $MgSO_4$. Volatile materials were removed under reduced pressure to give the corresponding oxime, which was used for the next acetylation step without further purification. The oxime crude material in pyridine (10 mL) was treated with acetic anhydride (2.0 mL, 21.7 mmol) and 4-(dimethylamino)pyridine (0.13 g, 1.1 mmol) stirred at room temperatrue for 1 h. The reaction mixture was then quenched with water and extracted twice with ethyl acetate. The combined organic extracts were washed with 1 N aqueous HCl and brine and dried over anhydrous $MgSO_4$. Volatile materials were removed in vacuo, and the crude was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 90:10) to afford the indole *O*-acetyl oxime **5a** (2.72 g, 8.60 mmol) in 78% yield.

**(*E*)-*tert*-Butyl 2-(1-(acetoxyimino)ethyl)-1*H*-indole-1-carboxylate (5a).** Prepared from 1-(1*H*-indol-2-yl)ethanone and purified by recrystallization from hexane/ethyl acetate (two times) in 78% yield. White solid; mp 62−64 °C; IR (NaCl) 1767, 1734, 1618, 1566, 1452, 1327 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.64 (9H, s), 2.26 (3H, s), 2.32 (3H, s), 6.77 (1H, s), 7.23−7.27 (1H, m), 7.36 (1H, ddd, $J$ = 1.2, 7.2, 8.4), 7.56 (1H, d, $J$ = 7.6 Hz), 8.09 (1H, dd, $J$ = 0.8, 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 18.5, 19.7, 28.0, 84.8, 111.8, 115.5, 121.4, 123.3, 125.5, 128.6, 133.9, 136.9, 149.4, 159.5, 168.5. ESIHRMS: found $m/z$ 317.1504, calcd for $C_{17}H_{21}N_2O_4$ $(M + H)^+$ 317.1501.

**(*E*)-*tert*-Butyl 2-(1-(acetoxyimino)pentyl)-1*H*-indole-1-carboxylate (5b).** Prepared from 1-(1*H*-indol-2-yl)pentan-1-one and purified by recrystallization from hexane/ethyl acetate (one time) in 36% yield. White solid; mp 81−83 °C; IR (NaCl) 2961, 1769, 1732, 1614, 1452, 1329 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.88 (3H, t, $J$ = 7.2 Hz), 1.32−1.37 (2H, m), 1.40−1.46 (2H, m), 1.63 (9H, s), 2.25 (3H, s), 2.74−2.78 (2H, m), 6.73 (1H, s), 7.24−7.27 (1H, m), 7.34−7.38 (1H, m), 7.56 (1H, d, $J$ = 7.6 Hz), 8.11 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 13.7, 19.7, 22.6, 27.96, 28.01, 31.5, 84.8, 112.3, 115.5, 121.3, 123.3, 125.4, 128.7, 132.6, 136.8, 150.0, 163.8, 168.6. ESIHRMS: found $m/z$ 359.1964, calcd for $C_{20}H_{27}N_2O_4$ $(M + H)^+$ 359.1971.

**Synthesis of 1-(1*H*-Indol-2-yl)pentan-1-one.** To a solution of 1*H*-indole-2-carboxylic acid (1.2 g, 7.5 mmol) in 25 mL of $Et_2O$ at 0 °C was added *n*-BuLi solution (14.0 mL, 22.4 mmol, 1.6 M in hexane) dropwise. The reaction mixture was allowed to stir for 1.5 h at reflux, then quenched with 1 N aqueous HCl, and extracted thrice with $Et_2O$. The combined organic extracts were washed with water and brine and dried over anhydrous $MgSO_4$. Volatile materials were removed under reduced pressure, and the resultant crude was purified by flash column

chromatography (silica gel, hexane/ethyl acetate = 90:10) to afford 1-(1*H*-indol-2-yl)pentan-1-one in 63% yield. Yellow solid; mp 113−115 °C; IR (NaCl) 3321, 3019, 1651, 1524, 1414, 1341, 1167, 1144 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.97 (3H, t, $J$ = 7.4 Hz), 1.44 (2H, tq, $J$ = 7.2, 7.6 Hz), 1.78 (2H, tt, $J$ = 7.2, 7.6 Hz), 2.95 (2H, t, $J$ = 7.6 Hz), 7.15 (1H, ddd, $J$ = 0.8, 6.8, 8.0 Hz), 7.21 (1H, m), 7.34 (1H, ddd, $J$ = 1.2, 7.2, 8.0 Hz), 7.43 (1H, d, $J$ = 8.4 Hz), 7.71 (1H, dd, $J$ = 0.8, 8.0 Hz), 9.11 (1H, br); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 13.9, 22.5, 27.3, 38.1, 109.1, 112.1, 120.9, 123.0, 126.2, 127.6, 135.2, 137.2, 183.7. ESIHRMS: found $m/z$ 202.1241, calcd for $C_{13}H_{16}NO$ $(M + H)^+$ 202.1232.

**(*E*)-*tert*-Butyl 2-(1-(Acetoxyimino)pent-4-enyl)-1*H*-indole-1-carboxylate (5c).** Prepared from 1-(1*H*-indol-2-yl)pent-4-en-1-one and purified by flash column chromatography (hexane/ethyl acetate = 5:95) in 55% yield. White solid; mp 61−63 °C; IR (NaCl) 2982, 1763, 1730, 1450, 1369, 1329 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.64 (9H, s), 2.19−2.23 (2H, m), 2.25 (3H, s), 2.87 (2H, m), 4.99 (1H, dd, $J$ = 1.3, 10.3 Hz), 5.02 (1H, dd, $J$ = 1.5, 17.2 Hz), 5.71−5.81 (1H, m), 6.74 (1H, s), 7.24−7.28 (1H, m), 7.36 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.56 (1H, d, $J$ = 7.6 Hz), 8.10 (1H, d, $J$ = 8.0 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 19.7, 28.0, 29.9, 31.1, 84.9, 112.5, 115.6, 115.8, 121.4, 123.3, 125.5, 128.6, 132.3, 136.5, 136.7, 149.5, 162.9, 168.5. ESIHRMS: found $m/z$ 357.1810, calcd for $C_{20}H_{25}N_2O_4$ $(M + H)^+$ 357.1814.

**Synthesis of 1-(1*H*-indol-2-yl)pent-4-en-1-one.** To a stirred suspension of Mg (0.7 g, 28.8 mmol) in anhydrous THF (30 mL) under $N_2$ atm was added 4-bromobut-1-ene (0.8 mL, 7.9 mmol) dropwise. Upon initiation, the remaining 4-bromobut-1-ene (1.7 mL, 16.4 mmol) was added dropwise, and the reaction mixture was allowed to reflux for 1.5 h. The solution was transferred via cannula to a solution of amide (0.8 g, 4.0 mmol) in anhydrous THF (8 mL) at 0 °C, and the reaction mixture was stirred for 24 h at room temperature. After completion, the resulting mixture was then quenched with 1 N aqueous HCl, then extracted with $Et_2O$, washed with water and brine, and dried over anhydrous $MgSO_4$. Volatile materials were removed in vacuo, and the resultant crude was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 90:10) to afford the desired ketone in 52% yield. Purple solid; mp 115−117 °C; IR (NaCl) 3310, 3017, 1651, 1524, 1416, 1341, 1142 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 2.52−2.58 (2H, m), 3.06 (2H, t, $J$ = 7.6 Hz), 5.03 (1H, dd, $J$ = 1.2, 10.0 Hz), 5.11 (1H, dd, $J$ = 1.6, 17.2 Hz), 5.87−5.96 (1H, m), 7.16 (1H, t, $J$ = 7.6 Hz), 7.23 (1H, d, $J$ = 1.2 Hz), 7.33−7.37 (1H, m), 7.43 (1H, d, $J$ = 8.0 Hz), 7.71 (1H, d, $J$ = 8.0 Hz), 9.18 (1H, br); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 28.8, 37.4, 109.2, 112.2, 115.5, 120.9, 123.0, 126.3, 127.6, 135.1, 137.0, 137.3, 192.5. ESIHRMS: found $m/z$ 200.1078, calcd for $C_{13}H_{14}NO$ $(M + H)^+$ 200.1075.

**(*Z*)-*tert*-Butyl 2-(1-(Acetoxyimino)-2-ethoxy-2-oxoethyl)-1*H*-indole-1-carboxylate (5d).** Prepared from *tert*-butyl 2-(2-ethoxy-2-oxoacetyl)-1*H*-indole-1-carboxylate via oximation followed by subsequent acetylation and purified by flash column chromatography (hexane/ethyl acetate = 5:95) in 30% yield. Yellow solid; mp 134−136 °C; IR (NaCl) 2980, 2936, 1771, 1728, 1717, 1607 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.37 (3H, t, $J$ = 7.2 Hz), 1.63 (9H, s), 2.20 (3H, s), 4.38 (2H, q, $J$ = 7.2 Hz), 6.91 (1H, s), 7.27−7.31 (1H, m), 7.41, (1H, ddd, $J$ = 1.2, 7.6, 8.8 Hz), 7.62 (1H, d, $J$ = 7.6 Hz), 8.11 (1H, d, $J$ = 8.4 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.0, 19.5, 27.9, 62.7, 85.6, 114.0, 115.5, 121.8, 123.3, 125.3, 126.1, 128.5, 135.9, 149.6, 150.0, 161.9, 167.7. ESIHRMS: found $m/z$ 375.1571, calcd for $C_{19}H_{23}N_2O_6$ $(M + H)^+$ 375.1556.

**Synthesis of *tert*-Butyl 2-(2-Ethoxy-2-oxoacetyl)-1*H*-indole-1-carboxylate.** To a solution of LDA freshly prepared from *n*-BuLi (4.9 mL, 7.8 mmol) and $HN(i\text{-}Pr)_2$ (1.1 mL, 7.8 mmol) in THF (16 mL) at −78 °C was added a solution of *tert*-butyl 1*H*-indole-1-carboxylate (1.6 g, 7.5 mmol) in THF (2 mL). The reaction was allowed to stir for 1 h at −78 °C before being transferred via cannula to a solution of diethyl oxalate (1.5 mL, 11.2 mmol) in THF (12 mL) at −78 °C. The reaction mixture was allowed to slowly warm to room temperature while stirring for 4 h, then quenched with water, and extracted with diethyl ether. The combined organic extracts were washed with water and brine and dried over anhydrous $MgSO_4$. Volatile materials were removed in vacuo, and the crude material was purified by flash column chromatography (silica gel, hexane/ethyl acetate = 90:10) to afford ethyl 2-(1*H*-indol-2-yl)-2-oxoacetate in 67% yield. Yellow solid; mp 81−83 °C; IR (NaCl) 1717, 1686, 1541, 1369, 1304, 1225, 1144, 1125 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.39 (3H, t, $J$ = 7.2 Hz), 1.65 (9H, s), 4.37 (2H, q, $J$ = 7.1 Hz), 7.30 (1H, ddd, $J$ = 0.8, 6.4, 8.8 Hz), 7.48 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.67 (1H, d, $J$ = 7.6 Hz), 8.02 (1H, dd, $J$ = 0.8, 8.4 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.0, 28.0, 62.5, 86.0, 115.4, 117.5, 123.0, 123.7, 127.9, 128.0, 135.2, 137.1, 150.2, 161.3, 178.0. ESIHRMS: found $m/z$ 318.1353, calcd for $C_{17}H_{20}NO_5$ $(M + H)^+$ 318.1341.

**(*E*)-*tert*-Butyl 2-((Acetoxyimino)methyl)-1*H*-indole-1-carboxylate (5e).** Prepared from 1*H*-indole-2-carbaldehyde and purified by recrystallization from hexane/ethyl acetate (one time) in 49% yield. White solid; mp 113−114 °C; IR (NaCl) 2982, 1767, 1734, 1553, 1449, 1329 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.71 (9H, s), 2.23 (3H, s), 7.25−7.29 (1H, m), 7.31 (1H, s), 7.38 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.60 (1H, d, $J$ = 7.6 Hz), 8.08 (1H, dd, $J$ = 0.4, 8.4 Hz), 9.05 (1H, d, $J$ = 0.4 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 19.5, 28.2, 85.4, 112.5, 115.8, 121.9, 123.6, 126.2, 128.5, 129.7, 137.1, 150.1, 150.7, 168.5. ESIHRMS: found $m/z$ 303.1346, calcd for $C_{16}H_{19}N_2O_4$ $(M + H)^+$ 303.1345.

**Rh(III)-Catalyzed Synthesis of Isoquinolines. Typical Procedure for the Reaction of Isobutyrophenone *O*-Acetyl Oxime (1b) and Diphenylacetylene (2a) (Table 1, entry 4).** To a DMF solution (1.5 mL) of isobutyrophenone *O*-acetyl oxime (**1b**) (61.6 mg, 0.30 mmol) and diphenylacetylene (**2a**) (64.2 mg, 0.36 mmol) were added $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol) and $Cu(OAc)_2$ (5.5 mg, 0.03 mmol), and the reaction mixture was stirred at 60 °C under a nitrogen atmosphere for 4 h. After cooling to room temperature, the reaction was quenched with pH 9 buffer, and organic materials were extracted three times with ethyl acetate. The combined extracts were washed with water (three times) and brine and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the crude was purified by flash column chromatography (hexane/ethyl acetate = 8:92) to afford 1-isopropyl-3,4-diphenylisoquinoline (**3ba**) (92.4 mg, 0.286 mmol) in 95% yield.

**1-Isopropyl-3,4-diphenylisoquinoline (3ba)[9b].** White solid; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.53 (6H, d, $J$ = 6.8 Hz),, 4.03 (1H, septet, $J$ = 6.8 Hz), 7.17−7.22 (3H, m), 7.23−7.25 (2H, m), 7.34−7.40 (3H, m), 7.43−7.46 (2H, m), 7.53−7.60 (2H, m), 7.66−7.68 (1H, m), 8.29−8.31 (1H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 22.3, 31.3, 124.5, 124.8, 126.2, 126.5, 126.8, 127.1, 127.4, 128.3, 128.4, 129.3, 130.6, 131.4, 136.5, 138.1, 141.3, 148.6, 165.0.

**1-Isopropyl-3,4-bis(4-methoxyphenyl)isoquinoline (3bb).** White solid; mp 127−129 °C; IR (NaCl) 2965, 1609, 1514, 1439, 1389, 1287, 1246, 1177 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.53 (6H, d, $J$ = 6.8 Hz), 3.78 (3H, s), 3.87 (3H, s), 4.01 (1H, septet, $J$ = 6.8 Hz), 6.76 (2H, td, $J$ = 2.8, 9.2 Hz), 6.94 (2H, td, $J$ = 2.8, 8.8 Hz), 7.17 (2H, td, $J$ = 2.8, 8.4 Hz), 7.43 (2H, td, $J$ = 2.8, 9.2 Hz), 7.53 (2H, td, $J$ = 3.6, 9.6 Hz), 7.65−7.69 (1H, m), 8.25−8.28 (1H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 22.3, 31.3, 55.1, 55.2, 112.9, 113.9, 124.5, 124.6, 125.9, 126.4, 127.3, 129.2, 130.4, 131.8, 132.4, 134.0, 137.0, 148.2, 158.5, 158.6, 164.6. ESIHRMS: found $m/z$ 384.1969, calcd for $C_{26}H_{26}NO_2$ $(M + H)^+$ 384.1964.

**3,4-Bis(4-bromophenyl)-1-isopropylisoquinoline (3bc).** Yellow solid; mp 158−160 °C; IR (NaCl) 2967, 1570, 1504, 1489, 1387, 1265, 1011 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.52 (6H, d, $J$ = 6.8 Hz), 4.03 (1H, septet, $J$ = 6.8 Hz), 7.13 (2H, td, $J$ = 2.4, 8.4 Hz), 7.31 (2H, td, $J$ = 2.0, 8.8 Hz), 7.36 (2H, td, $J$ = 2.0, 8.8 Hz), 7.54 (2H, td, $J$ = 2.4, 8.4 Hz), 7.56−7.63 (3H, m), 8.28−8.33 (1H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 22.2, 31.3, 121.5, 121.6, 124.7, 124.9, 126.1, 126.7,

127.2, 129.8, 130.8, 131.8, 132.1, 133.0, 136.2, 136.7, 139.9, 147.4, 165.6. ESIHRMS: found $m/z$ 481.9945, calcd for $C_{24}H_{20}N^{79}Br^{81}Br$ $(M + H)^+$ 481.9942.

**1-Isopropyl-3,4-dipropylisoquinoline (3bd)**[9b]**.** Colorless oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.03 (3H, t, $J$ = 7.2 Hz), 1.10 (3H, t, $J$ = 7.2 Hz), 1.42 (6H, d, $J$ = 6.8 Hz), 1.68 (2H, tt, $J$ = 7.2, 7.6 Hz), 1.86 (2H, tt, $J$ = 7.2, 7.6 Hz), 2.93 (2H, t, $J$ = 7.6 Hz), 2.98 (2H, t, $J$ = 7.6 Hz), 3.89 (1H, septet, $J$ = 6.8 Hz), 7.47 (1H, dd, $J$ = 7.6, 8.4 Hz), 7.62 (1H, dd, $J$ = 7.6, 8.4 Hz), 7.98 (1H, d, $J$ = 8.4 Hz), 8.18 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 14.7, 22.3, 23.0, 24.0, 29.8, 30.8, 37.1, 123.8, 124.5, 124.9, 125.0, 125.4, 128.8, 135.7, 151.5, 162.7.

**3,4-Bis((*tert*-butyldimethylsilyloxy)methyl)-1-isopropylisoquinoline (3be).** Pale yellow oil; IR (NaCl) 2955, 2928, 2857, 1566, 1472, 1462, 1389, 1360, 1254 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.06 (6H, s), 0.13 (6H, s), 0.89 (9H, t, $J$ = 2.4 Hz), 0.92 (9H, t, $J$ = 2.4 Hz), 1.41 (6H, d, $J$ = 6.8 Hz), 3.91 (1H, septet, $J$ = 6.8 Hz), 5.04 (2H, s), 5.25 (2H, s), 7.54 (1H, ddd, $J$ = 1.2, 6.8, 8.4 Hz), 7.66 (1H, ddd, $J$ = 1.2, 6.8, 8.4 Hz), 8.20 (1H, d, $J$ = 8.4 Hz), 8.27 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ −5.2, −5.0, 18.37, 18.41, 22.2, 25.95, 25.96, 31.0, 58.4, 66.6, 124.7, 125.2, 125.76, 125.79, 126.0, 129.0, 136.4, 149.7, 164.9. ESIHRMS: found $m/z$ 460.3086, calcd for $C_{26}H_{46}NO_2Si_2$ $(M + H)^+$ 460.3067.

**1-Isopropyl-4-methyl-3-phenylisoquinoline (3bf)**[9b]**.** White solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.47 (6H, d, $J$ = 6.8 Hz), 2.66 (3H, s), 3.95 (1H, septet, $J$ = 6.8 Hz), 7.40 (1H, tt, $J$ = 1.2, 7.2 Hz), 7.48 (2H, dd, $J$ = 7.2, 7.2 Hz), 7.59 (1H, $J$ = 8.0, 8.4 Hz), 7.66−7.74 (3H, m), 8.08 (1H, d, $J$ = 8.4 Hz), 8.27 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 15.7, 22.3, 31.1, 121.4, 124.4, 124.8, 125.1, 126.0, 127.3, 127.8, 129.3, 130.3, 136.8, 142.0, 150.2, 163.2.

**4-((*tert*-Butyldimethylsilyloxy)methyl)-1-isopropyl-3-phenylisoquinoline (3bg).** Yellow solid; mp 85−88 °C; IR (NaCl) 2959, 2928, 2857, 1614, 1564, 1504, 1470, 1389, 1256 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.15 (6H, s), 0.96 (9H, s), 1.48 (6H, d, $J$ = 6.8 Hz), 3.98 (1H, septet, $J$ = 6.8 Hz), 5.03 (2H, s), 7.44−7.52 (3H, m), 7.60 (1H, ddd, $J$ = 1.2, 6.8, 8.4 Hz), 7.74 (1H, ddd, $J$ = 1.2, 6.8, 8.4 Hz), 7.84−7.87 (2H, m), 8.27 (1H, d, $J$ = 8.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ −5.3, 18.4, 22.2, 25.9, 31.3, 60.4, 123.5, 124.9, 125.0, 125.3, 126.1, 127.8 (overlapped), 129.6, 130.3, 136.8, 141.0, 151.0, 165.5. ESIHRMS: found $m/z$ 392.2410, calcd for $C_{25}H_{34}NOSi$ $(M + H)^+$ 392.2410.

**Ethyl 1-Isopropyl-3-phenylisoquinoline-4-carboxylate (3bh).** White solid; mp 93−94 °C; IR (NaCl) 2968, 1717, 1570, 1557, 1504, 1449, 1389, 1265 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.07 (3H, t, $J$ = 7.2 Hz), 1.48 (6H, d, $J$ = 6.4 Hz), 4.00 (1H, septet, $J$ = 6.4 Hz), 4.26 (2H, q, $J$ = 7.2 Hz), 7.39−7.49 (3H, m), 7.62 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.73 (1H, ddd, $J$ = 1.2, 6.8, 8.4 Hz), 7.78−7.81 (2H, m), 8.05 (1H, d, $J$ = 8.4 Hz), 8.28 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 13.7, 22.1, 31.5, 61.6, 121.3, 124.3, 124.85, 124.88, 127.0, 128.2, 128.3, 129.0, 130.6, 133.9, 140.7, 149.2, 167.3, 169.5. ESIHRMS: found $m/z$ 320.1647, calcd for $C_{21}H_{22}NO_2$ $(M + H)^+$ 320.1651.

**Ethyl 1-Isopropyl-4-phenylisoquinoline-3-carboxylate (3bh-minor).** White solid; mp 92−93 °C; IR (NaCl) 2968, 2934, 1506, 1404, 1389, 1373, 1323, 1234 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.95 (3H, t, $J$ = 7.2 Hz), 1.51 (6H, d, $J$ = 6.8 Hz), 4.00 (1H, septet, $J$ = 6.8 Hz), 4.10 (2H, q, $J$ = 7.2 Hz), 7.35−7.37 (2H, m), 7.42−7.50 (3H, m), 7.58−7.67 (3H, m), 8.31 (1H, dd, $J$ = 2.4, 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 13.6, 22.1, 31.4, 61.0, 124.7, 126.5, 127.0, 127.7, 127.8, 128.1, 129.9, 130.1, 130.8, 135.7, 136.5, 141.9, 165.7, 168.1. ESIHRMS: found $m/z$ 320.1649, calcd for $C_{21}H_{22}NO_2$ $(M + H)^+$ 320.1651.

**4-Hexyl-1-isopropyl-3-(thiophen-2-yl)isoquinoline (3bi).** Yellow oil; IR (NaCl) 2961, 2928, 1560, 1506, 1468, 1447, 1431, 1387 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.95 (3H, t, $J$ = 7.2 Hz), 1.37−1.45 (4H, m), 1.48 (6H, d, $J$ = 6.8 Hz), 1.61 (2H, quintet, $J$ = 7.2 Hz), 1.78−1.86 (2H, m), 3.23−3.27 (2H, m), 3.91 (1H, septet, $J$ = 6.8 Hz), 7.17 (1H, dd, $J$ = 3.6, 5.2 Hz), 7.44 (1H, d, $J$ = 5.2 Hz), 7.46 (1H, d, $J$ = 3.6 Hz), 7.55 (1H, ddd, $J$ = 0.8, 6.8, 8.0 Hz), 7.70 (1H, ddd, $J$ = 1.2, 6.8, 8.4 Hz), 8.09 (1H, d, $J$ = 8.4 Hz), 8.22 (1H, d, $J$ = 8.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.1, 22.2, 22.7, 28.5, 29.8, 30.2, 31.1, 31.7, 124.4, 125.1, 125.2, 125.3, 125.4, 125.9, 127.1, 127.5, 129.5, 136.3, 142.6, 147.1, 163.1. ESIHRMS: found $m/z$ 338.1944, calcd for $C_{22}H_{28}NS$ $(M + H)^+$ 338.1942.

**1-*tert*-Butyl-3,4-diphenylisoquinoline (3ca).** White solid; mp 165−167 °C; IR (NaCl) 2984, 2968, 1547, 1506, 1476, 1396, 1368, 1194 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.76 (9H, s), 7.17−7.22 (3H, m), 7.27−7.29 (2H, m), 7.36−7.42 (3H, m), 7.48−7.56 (4H, m), 7.70−7.73 (1H, m), 8.59−8.62 (1H, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 31.3, 40.2, 124.5, 125.1, 126.8, 126.9, 127.06, 127.14, 127.4, 128.4, 128.6, 128.7, 130.6, 131.4, 137.6, 138.2, 141.2, 147.0, 165.8. ESIHRMS: found $m/z$ 338.1911, calcd for $C_{25}H_{24}N$ $(M + H)^+$ 338.1909.

**1-Benzyl-3,4-diphenylisoquinoline (3da).** White solid; mp 161−162 °C; IR (NaCl) 3019, 1612, 1601, 1568, 1551, 1495, 1449, 1371 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.51 (1H, s), 7.08−7.14 (3H,m), 7.21−7.33 (10H, m), 7.37−7.44 (7H, m), 7.48−7.55 (2H, m), 7.65−7.69 (1H, m), 8.28−8.32 (1H, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 55.1, 124.9, 125.7, 126.3, 126.5, 126.7, 126.9, 127.25, 127.27, 128.1, 128.4, 128.9, 129.5, 129.8, 130.6, 131.3, 136.9, 137.9, 140.7, 143.0, 148.0, 160.0. ESIHRMS: found $m/z$ 448.2066, calcd for $C_{34}H_{26}N$ $(M + H)^+$ 448.2065.

**1-Cyclopropyl-3,4-diphenylisoquinoline (3ea).** White solid; mp 149−151 °C; IR (NaCl) 1568, 1549, 1504, 1414, 1321, 1030, 1015 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.12−1.16 (2H, m), 1.38−1.42 (2H, m), 2.80−2.87 (1H, m), 7.15−7.20 (3H, m), 7.21−7.24 (2H, m), 7.33−7.39 (5H, m), 7.55−7.63 (2H, m), 7.65−7.67 (1H, m), 8.50 (1H, dd, $J$ = 1.6, 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 9.4, 13.6, 124.8, 126.23, 126.26, 126.34, 126.8, 127.1, 127.3, 128.0, 128.3, 129.6, 130.4, 131.4, 136.1, 138.0, 141.2, 148.7, 160.6. ESIHRMS: found $m/z$ 322.1600, calcd for $C_{24}H_{20}N$ $(M + H)^+$ 322.1596.

**(*E*)-3,4-Diphenyl-1-(prop-1-enyl)isoquinoline ((*E*)-3ea′).** White solid; mp 147−149 °C; IR (NaCl) 3075, 1653, 1541, 1503, 1445, 1385, 962 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.09 (3H, dd, $J$ = 1.6, 6.8 Hz), 7.18−7.26 (6H, m), 7.33−7.39 (4H, m), 7.39−7.42 (2H, m), 7.55−7.59 (2H, m), 7.65−7.68 (1H, m), 8.34−8.36 (1H, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 18.9, 124.6, 124.7, 126.1, 126.37, 126.43, 126.9, 127.1, 127.4, 128.2, 129.3, 129.7, 130.4, 131.4, 134.8, 136.7, 137.8, 141.2, 149.6, 154.2. ESIHRMS: found $m/z$ 322.1595, calcd for $C_{24}H_{20}N$ $(M + H)^+$ 322.1596.

**(*Z*)-3,4-Diphenyl-1-(prop-1-enyl)isoquinoline ((*Z*)-3ea′).** White solid; mp 125−127 °C; IR (NaCl) 1653, 1543, 1504, 1445, 1385, 963 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.07 (3H, dd, $J$ = 2.0, 7.2 Hz), 6.31 (1H, qd, $J$ = 7.2, 11.6 Hz), 7.15−7.24 (4H, m), 7.24−7.28 (2H, m), 7.34−7.42 (6H, m), 7.55−7.60 (2H, m), 7.67−7.70 (1H, m), 8.22−8.24 (1H, m); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 15.7, 125.8, 126.0, 126.1, 126.4, 126.9, 127.2, 127.5, 128.3, 129.8, 130.4, 131.4, 133.5, 136.4, 137.7, 141.1, 149.5, 156.1. ESIHRMS: found $m/z$ 322.1599, calcd for $C_{24}H_{20}N$ $(M + H)^+$ 322.1596.

***tert*-Butyl 1-Methyl-3,4-diphenyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6aa).** White solid; mp 155−156 °C; IR (NaCl) 1730, 1605, 1570, 1300, 1246, 1096 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.75 (9H, s), 2.89 (3H, s), 6.83 (1H, d, $J$ = 7.5 Hz), 7.01−7.05 (1H, m), 7.17−7.23 (3H, m), 7.29−7.32 (2H, m), 7.38−7.40 (5H, m), 7.46 (1H, ddd, $J$ = 1.2, 7.3, 8.4 Hz), 8.13 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 24.9, 28.2, 84.7, 115.1, 122.9, 123.3, 124.7, 126.97, 127.00, 127.6, 127.7, 128.6, 128.8, 130.1, 130.5, 132.5, 133.3, 137.6, 140.2, 141.0, 145.2, 150.4, 151.0. ESIHRMS: found $m/z$ 435.2088, calcd for $C_{29}H_{27}N_2O_2$ $(M + H)^+$ 435.2073.

**(*E*)-*tert*-Butyl 2-(1-(Hydroxyimino)ethyl)-1*H*-indole-1-carboxylate (7a).** Yellow solid; mp 148−151 °C; IR (NaCl) 3019, 1730, 1454, 1371, 1331, 1161, 1136 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.64 (9H, s), 2.20 (3H, s), 6.64 (1H, d, $J$ = 0.4 Hz),

7.22−7.24 (1H, m), 7.34 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.55 (1H, d, $J$ = 7.6 Hz), 8.03 (1H, br), 8.13 (1H, dd, $J$ = 0.4, 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 16.3, 28.0, 84.4, 110.3, 115.5, 121.1, 123.1, 125.1, 128.8, 136.0, 137.0, 149.7, 152.9. ESIHRMS: found $m/z$ 275.1402, calcd for $C_{15}H_{19}N_2O_3$ $(M + H)^+$ 275.1396.

***tert*-Butyl 3,4-Bis(4-methoxyphenyl)-1-methyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6ab).** White solid; mp 176−178 °C; IR (NaCl) 3019, 2980, 1730, 1609, 1514, 1458, 1429, 1369, 1298, 1246, 1152, 1034 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.74 (9H, s), 2.86 (3H, s), 3.77 (3H, s), 3.88 (3H, s), 6.73−6.76 (2H, m), 6.91−6.96 (3H, m), 7.03−7.07 (1H, m), 7.19−7.22 (2H, m), 7.32−7.35 (2H, m), 7.45 (1H, ddd, $J$ = 1.2, 7.6, 8.4 Hz), 8.12 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 24.9, 28.2, 55.2, 55.3, 84.6, 113.1, 114.2, 115.2, 122.8, 123.4, 124.9, 126.4, 128.7, 130.1, 131.3, 131.6, 132.9, 133.0, 133.1, 141.1, 144.9, 150.5, 151.0, 158.7, 159.1. ESIHRMS: found $m/z$ 495.2284, calcd for $C_{31}H_{31}N_2O_4$ $(M + H)^+$ 495.2284.

***tert*-Butyl 3,4-Bis(4-bromophenyl)-1-methyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6ac).** White solid; mp 188−190 °C; IR (NaCl) 3019, 2982, 1732, 1607, 1576, 1427, 1369, 1337, 1248, 1152, 1094, 1013 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.74 (9H, s), 2.87 (3H, s), 6.89 (1H, d, $J$ = 8.0 Hz), 7.09 (1H, t, $J$ = 7.6 Hz), 7.18 (2H, d, $J$ = 8.0 Hz), 7.24 (2H, d, $J$ = 8.8 Hz), 7.36 (2H, d, $J$ = 8.4 Hz), 7.47−7.51 (1H, m), 7.56 (2H, d, $J$ = 8.4 Hz), 8.13 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 24.9, 28.2, 85.0, 115.3, 121.6, 122.2, 123.1, 124.2, 125.6, 129.1, 131.0, 131.7, 132.1, 132.2, 132.3, 133.4, 136.3, 138.8, 141.0, 145.8, 149.6, 150.2. ESIHRMS: found $m/z$ 591.0285, calcd for $C_{29}H_{25}Br_2N_2O_2$ $(M + H)^+$ 591.0283.

***tert*-Butyl 1-Methyl-3,4-dipropyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6ad).** Yellow oil; IR (NaCl) 1732, 1609, 1578, 1246, 1121, 1090 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.06 (3H, t, $J$ = 7.2 Hz), 1.15 (3H, t, $J$ = 7.2 Hz), 1.69 (9H, s), 1.73−1.81 (4H, m), 2.72 (3H, s), 2.90−2.94 (2H, m), 3.07−3.11 (2H, m), 7.35 (1H, t, $J$ = 7.4 Hz), 7.51 (1H, t, $J$ = 7.6 Hz), 8.00 (1H, d, $J$ = 7.6 Hz), 8.15 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.4, 14.5, 23.0, 24.1, 24.5, 28.2, 30.9, 36.7, 84.4, 115.3, 123.17, 123.24, 124.8, 126.2, 128.2, 131.8, 132.9, 140.8, 143.0, 150.5, 153.4. ESIHRMS: found $m/z$ 367.2391, calcd for $C_{23}H_{31}N_2O_2$ $(M + H)^+$ 367.2386.

***tert*-Butyl 1,4-Dimethyl-3-phenyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6af).** Yellow solid; mp 140−141 °C; IR (NaCl) 1721, 1609, 1572, 1258, 1244, 1084 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.73 (9H, s), 2.77 (3H, s), 2.80 (3H, s), 7.38−7.44 (2H, m), 7.46−7.49 (2H, m), 7.57−7.61 (3H, m), 8.20 (2H, d, $J$ = 9.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 17.1, 24.7, 28.1, 84.6, 115.2, 121.6, 123.1, 123.6, 125.4, 127.5, 128.1, 128.5, 129.8, 132.7, 133.1, 140.6, 140.9, 143.1, 150.4, 152.6. ESIHRMS: found $m/z$ 373.1923, calcd for $C_{24}H_{25}N_2O_2$ $(M + H)^+$ 373.1916.

***tert*-Butyl 1,3-Dimethyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6af-minor).** Yellow oil; IR (NaCl) 2980, 2934, 1726, 1607, 1570, 1440, 1369, 1327, 1304, 1248, 1146, 1113 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.72 (9H, s), 2.32 (3H, s), 2.81 (3H, s), 6.70 (1H, dd, $J$ = 0.4, 8.0 Hz), 6.99−7.03 (1H, m), 7.34−7.37 (2H, m), 7.43 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.52−7.58 (3H, m), 8.08 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 22.1, 24.6, 28.2, 84.5, 115.1, 122.8, 123.1, 124.5, 127.3, 127.9, 128.7, 129.1, 129.4, 132.1, 132.6, 138.0, 141.0, 144.6, 149.2, 150.5. ESIHRMS: found $m/z$ 373.1910, calcd for $C_{24}H_{25}N_2O_2$ $(M + H)^+$ 373.1916.

***tert*-Butyl 4-((*tert*-Butyldimethylsilyloxy)methyl)-1-methyl-3-phenyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6ag).** Yellow solid; mp 54−55 °C; IR (NaCl) 1728, 1609, 1566, 1254, 1240, 1084 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.02 (6H, s), 0.86 (9H, s), 1.72 (9H, s), 2.82 (3H, s), 5.06 (2H, s), 7.37−7.48 (4H, m), 7.59 (1H, dd, $J$ = 7.6, 8 Hz), 7.65 (2H, d, $J$ = 6.8 Hz), 8.17 (1H, d, $J$ = 8.4 Hz), 8.36 (1H, d, $J$ = 7.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 18.2, 25.0, 25.8, 28.2, 60.3, 84.7, 115.0, 123.1, 123.3, 124.3, 125.0, 127.9, 128.1, 128.9, 129.9, 133.7, 133.8, 140.1, 141.0, 145.4, 150.3, 152.9. ESIHRMS: found $m/z$ 503.2720, calcd for $C_{30}H_{39}N_2O_3Si$ $(M + H)^+$ 503.2730.

***tert*-Butyl 3-((*tert*-Butyldimethylsilyloxy)methyl)-1-methyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6ag-minor).** Yellow solid; mp 118−120 °C; IR (NaCl) 1732, 1607, 1578, 1254, 1146, 1072 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ −0.01 (6H, s), 0.82 (9H, s), 1.73 (9H, s), 2.83 (3H, s), 4.70 (2H, s), 6.67 (1H, d, $J$ = 7.6 Hz), 7.01 (1H, t, $J$ = 7.6 Hz), 7.40−7.45 (3H, m), 7.51−7.54 (3H, m), 8.08 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 18.4, 24.7, 26.0, 28.2, 64.9, 84.6, 115.0, 122.9, 123.1, 124.5, 128.0, 128.2, 128.65, 128.69, 129.9, 132.3, 133.5, 136.8, 140.9, 144.8, 150.1, 150.4. ESIHRMS: found $m/z$ 503.2730, calcd for $C_{30}H_{39}N_2O_3Si$ $(M + H)^+$ 503.2730.

**9-*tert*-Butyl 4-Methyl 1-Methyl-3-phenyl-9*H*-pyrido[3,4-b]-indole-4,9-dicarboxylate (6aj).** Pale yellow solid; mp 115−117 °C; IR (NaCl) 1728, 1609, 1564, 1229, 1209, 1109 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.72 (9H, s), 2.86 (3H, s), 3.79 (3H, s), 7.35−7.43 (4H, m), 7.45−7.49 (1H, m), 7.61 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.69−7.72 (1H, m), 8.02 (1H, d, $J$ = 7.6 Hz), 8.17 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 25.2, 28.1, 52.6, 85.1, 115.3, 118.0, 122.7, 122.9, 123.5, 128.3, 128.4, 128.5, 129.9, 131.1, 133.1, 139.9, 141.2, 147.6, 150.0, 150.3, 169.4. ESIHRMS: found $m/z$ 417.1798, calcd for $C_{25}H_{25}N_2O_4$ $(M + H)^+$ 417.1814.

**9-*tert*-Butyl 3-Methyl 1-Methyl-4-phenyl-9*H*-pyrido[3,4-*b*]indole-3,9-dicarboxylate (6aj-isomer).** Pale yellow solid; mp 154−155 °C; IR (NaCl) 1734, 1607, 1570, 1233, 1217,1109 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.74 (9H, s), 2.90 (3H, s), 3.75 (3H, s), 6.72 (1H, d, $J$ = 7.6 Hz), 7.06 (1H, ddd, $J$ = 0.9, 7.2, 8.1 Hz), 7.38−7.40 (2H, m), 7.49 (1H, ddd, $J$ = 1.2, 7.6, 8.8 Hz), 7.52−7.56 (3H, m), 8.09 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 24.9, 28.1, 52.4, 85.4, 114.8, 123.2, 123.4, 123.9, 128.2, 128.7, 128.8, 129.3, 130.3, 132.3, 135.0, 136.7, 140.8, 140.9, 145.5, 149.9, 166.7. ESIHRMS: found $m/z$ 417.1833, calcd for $C_{25}H_{25}N_2O_4$ $(M + H)^+$ 417.1814.

***tert*-Butyl 1-Butyl-3,4-dipropyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6bd).** Yellow oil; IR (NaCl) 2959, 2930, 2870, 1732, 1607, 1572, 1464, 1431, 1391, 1369, 1153 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.90 (3H, t, $J$ = 7.4 Hz), 1.04 (3H, t, $J$ = 7.2 Hz), 1.16 (3H, t, $J$ = 7.4 Hz), 1.27−1.36 (2H, m), 1,66−1.86 (6H, m), 1.71 (9H, s), 2.89−2.93 (2H, m), 3.08−3.14 (4H, m), 7.35−7.39 (1H, m), 7.50−7.55 (1H, m), 8.02 (1H, d, $J$ = 8.0 Hz), 8.14 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.0, 14.3, 14.5, 22.88, 22.94, 23.7, 28.2, 30.3, 30.9, 36.5, 36.8, 84.2, 115.2, 123.1, 123.2, 125.0, 126.1, 128.1, 131.8, 132.3, 140.9, 147.0, 150.7, 153.3. ESIHRMS: found $m/z$ 409.2849, calcd for $C_{26}H_{37}N_2O_2$ $(M + H)^+$ 409.2855.

***tert*-Butyl 1-(But-3-enyl)-3,4-dipropyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6 cd).** Yellow oil; IR (NaCl) 3019, 2961, 2932, 2872, 1728, 1639, 1607, 1572, 1464, 1431, 1371, 1153, 1121 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (3H, t, $J$ = 7.2 Hz), 1.16 (3H, t, $J$ = 7.4 Hz), 1.70 (9H, s), 1.73−1.84 (4H, m), 2.51−2.57 (2H, m), 2.90−2.94 (2H, m), 3.09−3.13 (2H, m), 3.16−3.20 (2H, m), 4.90 (1H, dd, $J$ = 0.8, 10.0 Hz), 5.02 (1H, dd, $J$ = 1.6, 17.2 Hz), 5.81−5.91 (1H, m), 7.38 (1H, t, $J$ = 7.6 Hz), 7.53 (1H, t, $J$ = 7.8 Hz), 8.02 (1H, d, $J$ = 8 Hz), 8.14 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 14.5, 22.9, 23.6, 28.2, 30.9, 32.1, 36.1, 36.4, 84.4, 114.3, 115.3, 123.1, 123.2, 125.0, 126.3, 128.1, 131.9, 132.4, 138.7, 140.9, 145.9, 150.8, 153.3. ESIHRMS: found $m/z$ 407.2696, calcd for $C_{26}H_{35}N_2O_2$ $(M + H)^+$ 407.2699.

**9-*tert*-Butyl 1-Ethyl 3,4-Dipropyl-9*H*-pyrido[3,4-*b*]indole-1,9-dicarboxylate (6dd).** Yellow solid; mp 43−45 °C IR (NaCl) 3019, 2965, 1736, 1609, 1574, 1464, 1396, 1371, 1344, 1314, 1153, 1125 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (3H, t, $J$ = 7.6 Hz), 1.17 (3H, t, $J$ = 7.6 Hz), 1.43 (3H, t, $J$ = 7.2 Hz), 1.69 (9H, s), 1.73−1.83 (4H, m), 2.97−3.00 (2H, m), 3.15−3.19 (2H, m), 4.48 (2H, q, $J$ = 7.2 Hz), 7.41 (1H, dd, $J$ = 0.8, 8 Hz), 7.58 (1H, dd, $J$ = 0.8, 8,4 Hz), 8.05 (1H, d, $J$ = 8.0 Hz), 8.17 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.2, 14.3, 14.5, 22.6, 23.8, 28.1, 31.1, 36.5, 61.5, 84.9, 115.9,

123.3, 123.5, 124.1, 128.8, 131.3, 131.5, 132.5, 136.7, 140.1, 150.6, 153.6, 166.8. ESIHRMS: found $m/z$ 425.2438, calcd for $C_{25}H_{33}N_2O_4$ $(M + H)^+$ 425.2440.

***tert*-Butyl 3,4-Dipropyl-9*H*-pyrido[3,4-*b*]indole-9-carboxylate (6ed).** Yellow solid; mp 42−43 °C IR (NaCl) 2961, 2932, 2872, 1730, 1611, 1462, 1433, 1346, 1325, 1157, 1123 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.05 (3H, t, $J$ = 7.2 Hz), 1.16 (3H, t, $J$ = 7.2 Hz), 1.71−1.83 (4H, m), 1.75 (9H, s), 2.93−2.97 (2H, m), 3.11−3.15 (2H, m), 7.38 (1H, t, $J$ = 7.6 Hz), 7.56 (1H, dd, $J$ = 7.6, 8.4 Hz), 8.02 (1H, d, $J$ = 8.0 Hz), 8.49 (1H, d, 8.4 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 14.4, 22.7, 23.8, 28.3, 31.1, 36.5, 84.5, 116.4, 123.1, 123.3, 124.2, 128.5, 128.9, 130.3, 133.4, 135.0, 139.5, 150.4, 153.3. ESIHRMS: found $m/z$ 353.2232, calcd for $C_{22}H_{29}N_2O_2$ $(M + H)^+$ 353.2229.

***tert*-Butyl 2-Cyano-1*H*-indole-1-carboxylate (8).** White solid; mp 102−104 °C; IR (NaCl) 3019, 2984, 2230, 1741, 1535, 1445, 1373, 1344, 1325, 1155, 1123, 1092 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.73 (9H, s), 7.31−7.35 (2H, m), 7.50 (1H, ddd, $J$ = 0.8, 7.2, 8.4 Hz), 7.63 (1H, d, $J$ = 8.0 Hz), 8.24 (1H, d, $J$ = 8.8 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 28.0, 86.7, 108.9, 113.3, 115.9, 121.5, 122.1, 124.1, 127.3, 128.2, 136.6, 148.2. ESIHRMS: found $m/z$ 243.1141, calcd for $C_{14}H_{15}N_2O_2$ $(M + H)^+$ 243.1134.

**1-Methyl-3,4-dipropylbenzofuro[2,3-*c*]pyridine (6fd).** White solid; mp 60−62 °C; IR (NaCl) 2959, 2930, 2870, 1628, 1599, 1464, 1435, 1109 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.05 (3H, t, $J$ = 7.2 Hz), 1.14 (3H, t, $J$ = 7.2 Hz), 1.71−1.82 (4H, m), 2.88−2.92 (2H, m), 3.06 (2H, m), 7.39 (1H, ddd, $J$ = 0.8, 7.6, 8.4 Hz), 7.55 (1H, ddd, $J$ = 1.2, 7.2, 8.4 Hz), 7.63 (1H, d, $J$ = 8.0 Hz), 7.98 (1H, d, $J$ = 8.0 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 14.4, 18.5, 23.2, 24.2, 31.3, 36.5, 112.3, 123.0, 123.28, 123.33, 127.6, 128.6, 129.1, 139.6, 149.8, 152.6, 156.6. ESIHRMS: found $m/z$ 268.1699, calcd for $C_{18}H_{22}NO$ $(M + H)^+$ 268.1701.

**7-Methyl-4,5-dipropyl-1-tosyl-1*H*-pyrrolo[2,3-*c*]pyridine (6gd).** White solid; mp 78−80 °C; IR (NaCl) 2961, 2932, 1576, 1454, 1445, 1368, 1173, 1132 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.98 (3H, t, $J$ = 7.2 Hz), 0.99 (3H, t, $J$ = 7.2 Hz), 1.55−1.73 (4H, m), 2.38 (3H, s), 2.71 (3H, s), 2.72−2.78 (4H, m), 6.67 (1H, d, $J$ = 4.0 Hz), 7.25 (1H, d, $J$ = 9.2 Hz), 7.58 (1H, d, $J$ = 8.4 Hz), 7.86 (1H, d, $J$ = 3.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.28, 14.32, 21.6, 23.7, 24.0, 24.7, 30.8, 36.3, 106.0, 124.6, 126.6, 129.96, 130.01, 132.0, 136.6, 138.9, 141.5, 144.9, 151.9. ESIHRMS: found $m/z$ 371.1783, calcd for $C_{21}H_{27}N_2O_2S$ $(M + H)^+$ 371.1793.

**7-Methyl-4,5-dipropylfuro[2,3-*c*]pyridine (6hd).** Yellow oil; IR (NaCl) 2961, 2932, 2870, 1614, 1587, 1450, 1377, 1192, 1152 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.98−1.03 (6H, m), 1.60−1.67 (2H, m), 1.69−1.77 (2H, m), 2.70 (3H, s), 2.76−2.84 (4H, m), 6.74 (1H, d, $J$ = 2.4 Hz), 7.65 (1H, d, $J$ = 2.4 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 18.3, 24.0, 24.2, 31.5, 36.5, 105.2, 125.4, 133.8, 139.2, 146.8, 149.3, 151.6. ESIHRMS: found $m/z$ 218.1547, calcd for $C_{14}H_{20}NO$ $(M + H)^+$ 218.1545.

**7-Methyl-4,5-dipropylthieno[2,3-*c*]pyridine (6id).** Yellow oil; IR (NaCl) 2959, 2930, 2870, 1557, 1454, 1425, 1379, 1362, 1165 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.03 (3H, t, $J$ = 7.6 Hz), 1.03 (3H, t, $J$ = 7.6 Hz), 1.61−1.70 (2H, m), 1.71−1.80 (2H, m), 2.74 (3H, s), 2.84−2.91 (4H, m), 7.38 (1H, d, $J$ = 5.6 Hz), 7.59 (1H, d, $J$ = 5.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.3, 14.4, 23.3, 24.1, 24.3, 31.7, 36.6, 122.4, 126.6, 130.2, 133.1, 145.3, 149.4, 153.0. ESIHRMS: found $m/z$ 234.1322, calcd for $C_{14}H_{20}NS$ $(M + H)^+$ 234.1316.

## ■ ASSOCIATED CONTENT

**Supporting Information.** Investigation of reaction mechanism and NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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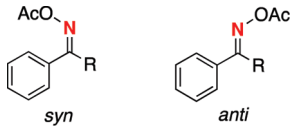


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(14) Narasaka reported Pd(0)-catalyzed amino-Heck reactions of alkenyl *O*-acyloximes, where both *syn*- and *anti*-oximes could be employed for cyclization (see ref 11c). Hartwig isolated iminyl Pd(II) species generated via oxidative addition of the N−O bond of *O*-pentafluorobenzoyloxime to a Pd(0) complex and characterized its structure by X-ray crystallographic analysis, which revealed that the bond angle of C═N−Pd is about 120° (see ref 11a). On the basis of these results, iminyl Pd(II) species should be free to isomerize between *syn*- and *anti*-isomers.

(15) Liebeskind reported synthesis of *N*-substituted imines by copper-catalyzed N-imination of boronic acids with *O*-acyloximes via putative iminyl copper species (see ref 12b). Separate treatments of stereoisomeric *syn*- and *anti*-oximes derived from phenyl-2-furyl ketone with 3-hydroxyphenylboronic acid in the presence of $Cu(OAc)_2$ catalyst resulted in formation of the corresponding *N*-aryl imines with the same *E*/*Z* ratio, implying that there should be free isomerization between *anti*- and *syn*-forms of the iminyl copper species.

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(17) The UV−vis spectra for the treatment of $Cu^{II}(OAc)_2$ in DMF at 90 °C showed disappearance of the visible band of $Cu^{II}(OAc)_2$ at 700 nm within 30 min, implying that DMF might reduce $Cu^{II}(OAc)_2$ to form Cu(I) species. On the other hand, the UV−vis spectra for the treatment of $[Cp^*RhCl_2]_2$ in DMF at 90 °C showed no change of the visible band of $[Cp^*RhCl_2]_2$ at 410 nm; see Supporting Information.

(18) Treatment of oxime **1b** with 1.2 equiv of CuOAc in DMF at 60 °C afforded 22% yield of isobutyrophenone, which could be formed via hydrolysis of iminyl copper species **A** during the workup process.

(19) For ease of handling, $Cu^{II}(OAc)_2$ was mainly utilized as the catalyst because $Cu^{I}(OAc)$ is very sensitive to air, moisture, and light.

(20) We are not certain as to the reaction mechanism of the formation of alkenyl isoquinoline **3ea′**. Since no reaction was observed in the treatment of cyclopropyl isoquinoline **3ea** with the present reaction conditions, ring opening of the cyclopropane moeity might occur during the C−H bond activation/annulation processes. To confirm the ring-opening mechanism, we conduted the reactions of cyclopropyl oxime **2e** and alkyne **2a** in the presence of 2 equiv of $D_2O$ in DMF or in DMF-$d_7$. However, no duterium incorporation at the propenyl part of **3ea′** was observed from both experiments.

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