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Microwave-Assisted, Rhodium(III)-Catalyzed N-Annulation Reactions of Aryl and α,β-Unsaturated Ketones with Alkynes

Hyejeong Lee, Yong-Kyun Sim, Jung-Woo Park, and Chul-Ho Jun*[a]

Dedicated to Professor Teruaki Mukaiyama in celebration of the 40th anniversary of the Mukaiyama aldol reaction

Abstract: New Rh^{III}-catalyzed, one-pot N-annulation reactions of aryl and α,β-unsaturated ketones with alkynes in the presence of ammonium acetate have been developed. Under microwave irradiation conditions, the processes lead to rapid formation of the respective isoquinoline and pyridine derivatives with efficiencies that are strongly dependent on the steric nature of the aryl ring and enone substituents. By employing this protocol, a variety of isoquinoline and pyridine derivatives were prepared in high yields. In addition, a new one-pot approach to the synthesis of pyridines, involving four-component reactions of ketones, formaldehyde, NH_4OAc, and alkynes, has been uncovered. This process takes place through a route involving initial aldol condensation of the ketone with formaldehyde to generate a branched α,β-unsaturated ketone that then undergoes Rh^{III}-catalyzed N-annulation with NH_4OAc and the alkyne.

Introduction

The development of new methods for the synthesis of N-heterocyclic compounds, which utilize transition-metal-catalyzed C–H bond activation processes, is an important goal of synthetic organic chemists because processes of this type are typically highly chemoselective and atom-economic.[1] Particular interest in this area has focused on the synthesis of isoquinolines and pyridines owing to their biological properties and, consequently, their use in the pharmaceutical industry. Current synthetic protocols devised for the preparation of these nitrogen heterocycles utilize chelation-assisted, transition-metal-promoted C–H bond activation of a variety of different starting materials, including imines,[2] oximes,[3] and azides,[4] followed by ensuing N-annulation reactions. However, many of the previously developed N-annulation reactions possess several disadvantageous features, including the use of unstable preinstalled imine functionality and the limited availability of α,β-unsaturated imine reactants.[2,3] To overcome these problems, we recently developed two new methods for the synthesis of pyridines that utilize Rh^{III}/Cu^{II}-catalyzed reaction of an allylamine and alkyne,[5] and between α,β-enones, alkynes, and NH_4OAc.[6] The strategy used to design these reactions relied on observations made in our previous studies, which led to the development of a method for the synthesis of isoquinolines through sequential Rh^{I}-catalyzed *ortho*-alkenylation reactions of aryl ketimines followed by cyclization of the resulting *ortho*-alkenyl-aryl ketimines.[7]

The results of several studies have demonstrated that microwave irradiation serves as a good alternative to conventional heating to enhance the rates of chemical reactions.[8] In spite of the existing controversy about the origin of the effect,[9] microwave irradiation has become the accepted format for affecting specific types of organic reactions, such as by-product-free condensation processes. Because one of the steps in the new process we have developed involves a condensation reaction between a ketone and ammonia to give an imine, we have utilized microwave irradiation instead of conventional heating to promote the new N-annulation reaction developed in the current study.

Herein, we describe the results of an investigation that has resulted in the development of a new one-pot method for the facile synthesis of isoquinolines and pyridines. In this process, which involves Rh^{III}-catalyzed C–H activation and N-annulation steps, aryl and α,β-unsaturated ketones react with alkynes and NH_4OAc under microwave irradiation conditions to generate the respective isoquinolines and pyridines. In addition, this strategy has been applied in devising a new one-pot, four-component method for N-annulation reactions between alkyl ketones, formaldehyde, alkynes, and NH_4OAc.

Results and Discussion

The protocol for carrying out the Rh^{III}-catalyzed, microwave-assisted, one-pot, three-component annulation reaction, leading to the generation of isoquinolines, was investigated by using 4-methoxyacetophenone (**1a**) as the aryl ketone substrate. To determine the effect of microwaves as a heat source, we carried out comparison studies of N-annulation reactions under conventional heating and microwave irradiation. When the N-

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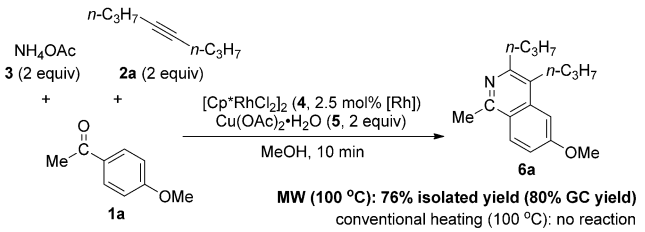
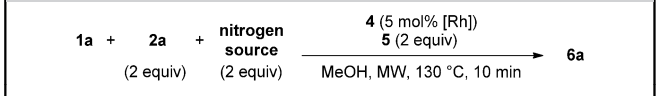
annulation reaction of **1a** was performed with 4-octyne (**2a**, 2 equiv) and ammonium acetate (**3**, 2 equiv) in the presence of $[Cp^*RhCl_2]_2$ (**4**, Cp^* = pentamethylcyclopentadienyl, 2.5 mol% [Rh]) and $Cu(OAc)_2 \cdot H_2O$ (**5**, 2.0 equiv) under microwave irradiation conditions (100 °C, 10 min), isoquinoline **6a** was isolated in 76% yield (80% yield determined by GC analysis), whereas the same reaction under conventional thermal heating conditions did not give any product (Scheme 1). This result indicates that the N-annulation proceeds in a much more facile manner under microwave irradiation than conventional heating.



Scheme 1. Comparison between MW and conventional heating for synthesis of **6a**.

Next, the reactions were carried out with various amines to find a suitable reagent for the nitrogen source under more intense reaction conditions (5 mol% **4**, 130 °C; Table 1). For example, the reaction of **1a**, **2a**, and NH_3 in the presence of **4** (5 mol% [Rh]) and **5** (2.0 equiv based on **1a**) under microwave irradiation conditions was observed to form **6a** in 97% yield of isolated product (Table 1, entry 1). The results of studies probing the use of other nitrogen sources for this process, such as NH_4OAc, NH_2OH,[6] $PhNHNH_2$, NH_2NH_2, NH_4NO_3, and NH_4Cl (Table 1, entries 2–8), showed that NH_4OAc (**3**) is ideal because it promotes efficient reactions (90%) and is an easily handled solid.

Table 1. Nitrogen sources for the N-annulation reaction of aryl ketone **1a** with alkyne **2a**.



Entry	Nitrogen source	Yield [%][a]
1	NH_3 (7.0 M solution in MeOH)	97
2	$NH_2OH \cdot HCl$	0
3	$H_2N–NH_2 \cdot x H_2O$	30
4	$PhNH–NH_2$	1
5	NH_4OAc (**3**)	90
6	NH_4Cl	17
7	NH_4NO_3	2
8	NH_4Cl + NaOAc	14

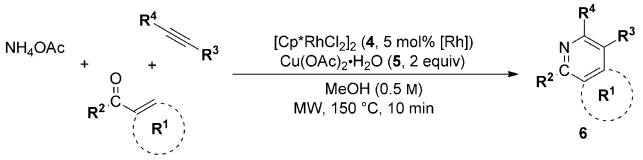
[a] Yields of isolated products.

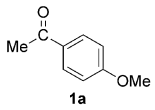
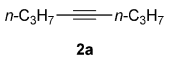
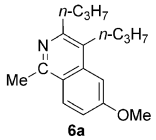
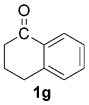
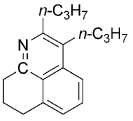
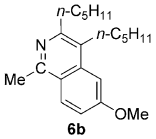
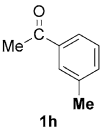
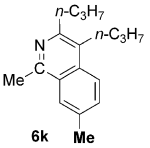
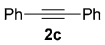
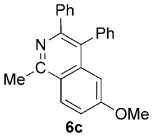
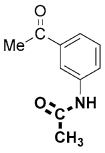
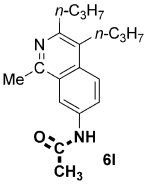
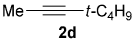
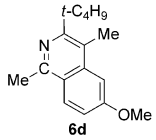
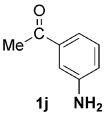
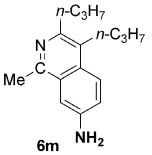
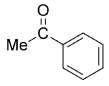
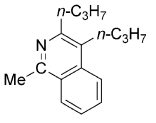
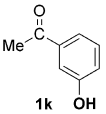
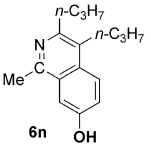
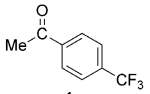
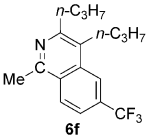
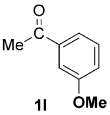
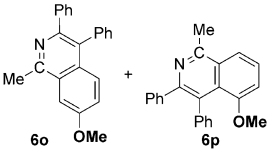
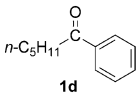
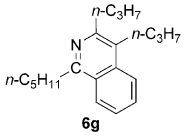
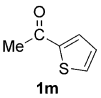
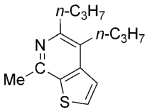
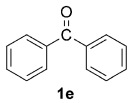
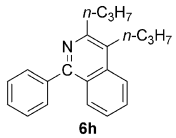
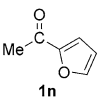
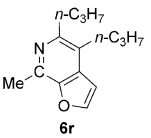
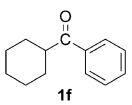
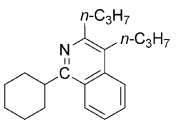
The scope of the N-annulation reaction was investigated with various aryl ketones, alkynes, and ammonium acetate as the nitrogen source (Table 2). The results of this effort demonstrated that reaction of **1a** with 4-octyne (**2a**) and NH_4OAc (**3**) in the presence of **4** (5 mol% [Rh]) and **5** (2 equiv) at 150 °C under microwave irradiation conditions produces the corresponding isoquinoline **6a** in 93% yield of isolated product (Table 2, entry 1). In addition, N-annulation reactions using both alkyl (**2b**) and aryl (**2c**) substituted alkynes take place to form the respective isoquinolines **6b** (94%) and **6c** (92%; Table 2, entries 2 and 3). Interestingly, reaction of the unsymmetric and sterically biased alkyne, 4,4-dimethylpent-2-yne (**2d**), generates isoquinoline **6d**, in which the bulky *tert*-butyl group is positioned at C3 exclusively with a 41% yield of isolated product (Table 2, entry 4). Other aryl ketones, such as acetophenone (**1b**), 4-trifluoromethyl acetophenone (**1c**), hexanophenone (**1d**), benzophenone (**1e**), cyclohexyl(phenyl)methanone (**1f**), and 3,4-dihydronaphthalen-1(2*H*)-one (**1g**), also participate in N-annulation reactions that produce the corresponding isoquinoline derivatives isolated in 90–97% yields (Table 2, entries 5–10).

To gain information about factors controlling the regioselectivity of the N-annulation process, studies were carried out with aryl ketones that contain *meta*-aryl ring substituents. Substrates of this type are interesting because they possess two different *ortho*-C–H bonds that can be activated in the initial carbometalation step of the reaction. Interestingly, N-annulation reaction of 3-methylacetophenone (**1h**) with 4-octyne (**2a**) and NH_4OAc was observed to form 1,7-dimethyl-3,4-dipropylisoquinoline (**6k**) exclusively (91% yield of isolated product, Table 2, entry 11), which demonstrates that only the C6 *ortho*-C–H bond of the aryl group is activated in this reaction. Thus, it appears that the regiochemical course of this process is guided by the steric influence of *meta* substituents. Moreover, reaction of *N*-(3-acetylphenyl)acetamide (**1i**) with **2a** exclusively forms the isoquinoline regioisomer **6l** (88% yield of isolated product, Table 2, entry 12). Likewise, 3-aminoacetophenone (**1j**) reacts with **2a** under these conditions to generate a mixture of *N*-(1-methyl-3,4-dipropylisoquinolin-7-yl)acetamide (**6l**) and 1-methyl-3,4-dipropylisoquinolin-7-amine (**6m**; Table 2, entry 13), both being produced through activation of the less sterically hindered aryl ketone C6 C–H bond. In this process, it is likely that acetamide **6l** is formed by acetylation of **6m** by NH_4OAc (**3**). The same regiochemical driving force operates in the reaction of 3-hydroxyacetophenone (**1k**) with **2a**, which results in formation of the single isoquinoline regioisomer **6n** (Table 2, entry 14). However, reaction of 3-methoxyacetophenone (**1l**) with **2a** was observed to yield a mixture of regioisomers, **6o** and **6p** in a 46:48 ratio (Table 2, entry 15). In this case, formation of **6p** is a consequence of the activating effect of the C3 methoxy group, which competes with its steric effect. The results of further studies show that heteroaromatic ketones also serve as substrates for the new N-annulation reaction. For example, 1-(thiophen-2-yl)ethanone (**1m**) and 1-(furan-2-yl)ethanone (**1n**) react with **2a** in the presence of **3**, **4** (5 mol% [Rh]), and **5** (2 equiv) under microwave irradiation conditions (150 °C) to generate the corresponding pyridines **6q** and **6r** in high yields (Table 2, entries 16 and 17).

Using the protocol described above, an investigation of N-annulation reactions of nonaromatic α,β-unsaturated ketones was carried out. The results of this effort demonstrate that,

Table 2. Substrate scope for the N-annulation reaction of aryl ketone **1**, alkyne **2**, and NH_4OAc (**3**).

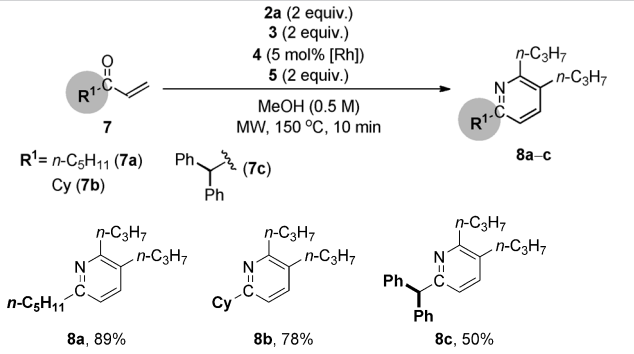


Entry	Aryl ketone **1**	Alkyne **2** (R^3 and R^4)	Product **6**	Yield [%][a]	Entry	Aryl ketone **1**	Alkyne **2** (R^3 and R^4)	Product **6**	Yield [%][a]
1	 **1a**	 **2a**	 **6a**	93 (>99)	10	 **1g**	**2a**	 **6j**	93 (>99)
2	**1a**	**2b**	 **6b**	94 (>99)	11	 **1h**	**2a**	 **6k**	91 (>99)
3	**1a**	 **2c**	 **6c**	92 (>99)	12	 **1i**	**2a**	 **6l**	88 (>99)
4	**1a**	 **2d**	 **6d**	41 (46)	13	 **1j**	**2a**	**6l** +  **6m**	**6l/6m** 50:27
5	 **1b**	**2a**	 **6e**	95 (98)	14	 **1k**	**2a**	 **6n**	66
6	 **1c**	**2a**	 **6f**	93 (97)	15	 **1l**	**2c**	 **6o** **6p**	**6o/6p** 46:48
7	 **1d**	**2a**	 **6g**	92 (>99)	16	 **1m**	**2a**	 **6q**	94 (>99)
8	 **1e**	**2a**	 **6h**	90 (>99)	17	 **1n**	**2a**	 **6r**	71 (78)
9	 **1f**	**2a**	 **6i**	97 (>99)					

[a] Yield of isolated product. Yields determined by GC analysis are given in parentheses.

under the conditions developed for reactions of aryl ketones, a variety of α,β-unsaturated ketones (**7**) react efficiently with alkynes (**2**) to generate substituted pyridines (Table 3). For example, the vinyl ketones oct-1-en-3-one (**7a**), 1-cyclohexyl-

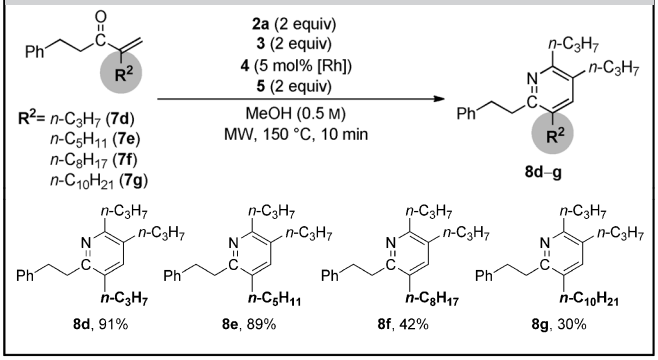
Table 3. Effects of carbonyl substituents (R^1) in **7** on the N-annulation reaction.



Cy = cyclohexyl.

prop-2-en-1-one (**7b**), and 1,1-diphenylbut-3-en-2-one (**7c**) participate in N-annulation reactions with 4-octyne that produce the respective pyridines **8a–c**, which were isolated in high yields (50–89%). In addition, vinyl ketones containing *n*-C_3H_7 (**7d**) and *n*-C_5H_{11} (**7e**) α substituents also undergo reactions with alkyne **2a** in the presence of the same catalytic system to form the corresponding pyridines **8d** and **8e** in high yields of isolated products (91% for **8d** and 89% for **8e**, Table 4). However, α,β-unsaturated ketones with long alkyl

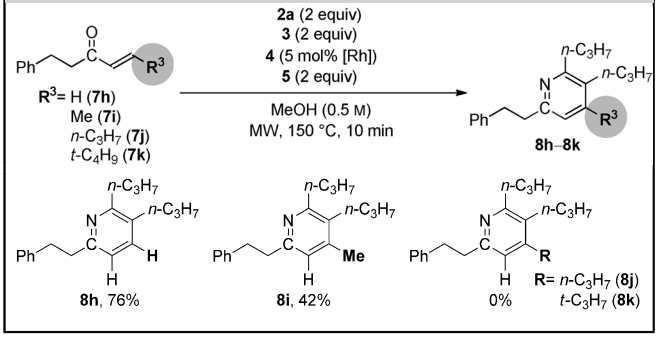
Table 4. Effects of α substituents (R^2) in **7** on the N-annulation reaction.



chains, such as *n*-C_8H_{17} (**7f**) and *n*-$C_{10}H_{21}$ (**7g**), at the α position undergo much less efficient annulation reactions that form the corresponding pyridine **8f** and **8g**, which were isolated in low yields (42% for **8f** and 30% for **8g**).

The β substituents have a pronounced effect on the N-annulation process (Table 5). Thus, in contrast to the reaction of the simple vinyl ketone **7h** with **2a** that produces pyridine **8h** in 76% yield of isolated product, the corresponding reaction of the β-methyl-substituted substrate **7i** with the same alkyne

Table 5. Effects of β substituents (R^3) in **7** on the N-annulation reaction.



(**2a**) in the presence of **3**, **4** (5 mol% [Rh]), and **5** (2 equiv) at 150 °C under microwave irradiation conditions forms pyridine **8i** in only 42% yield of isolated product. Finally, α,β-unsaturated ketones bearing *n*-propyl (**7j**) and *tert*-butyl (**7k**) groups at the β position do not serve as substrates for this process. The results suggest that the efficiency of the N-annulation reaction is strongly dependent on steric effects associated with the presence of β substituents on the α,β-enone in the following order: H > Me > *n*-C_3H_7 ≈ *t*-C_4H_9.

The N-annulation reaction is thought to proceed in the following sequence (Figure 1). First, imine **9** is generated by condensation of α,β-enone **7** with ammonia. Activation of the N–H bond in imine **9** by Rh^{III} gives iminorhodium(III) intermediate **10**. Then, Rh^{III}-promoted β-C–H bond activation in the intermediate **10** and subsequent coordination of alkyne **2a** affords rhodacyclic complex **A**. Carbometalation of alkyne in **A** gives rise to seven-membered rhodacycle **B**. Reductive elimination of **B** results in the formation of pyridine **8** and Rh^{I}. Catalytically active Rh^{III} complex is regenerated by Cu^{II}-promoted oxidation of the resulting Rh^{I} intermediate with **5**. In this process, it is

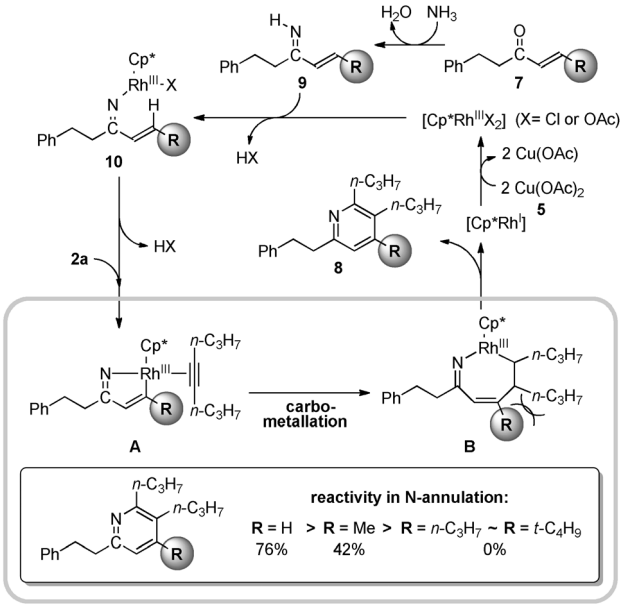
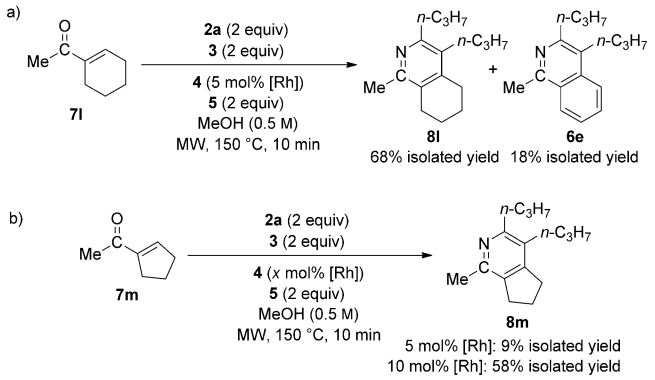


Figure 1. Proposed mechanism of the N-annulation reaction and origin of the steric effect of β substituent R on rhodacycle **B**.

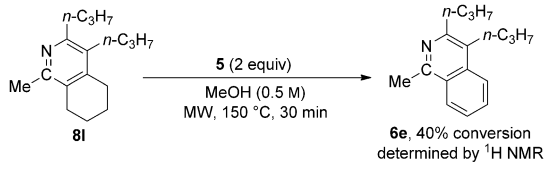
likely that bulky β substituents R, such as *n*-propyl and *tert*-butyl, retard the N-annulation reaction by causing steric interference in the alkyne carbometalation step transforming intermediate **A** to **B** (Figure 1).

1-Acylcycloalkenes are potentially interesting substrates for the N-annulation reaction because the process would lead to the generation of polycyclic pyridine derivatives (Scheme 2). To



Scheme 2. N-Annulation reactions of cyclic α,β-enones a) **7l** and b) **7m** with **2a** and **3**.

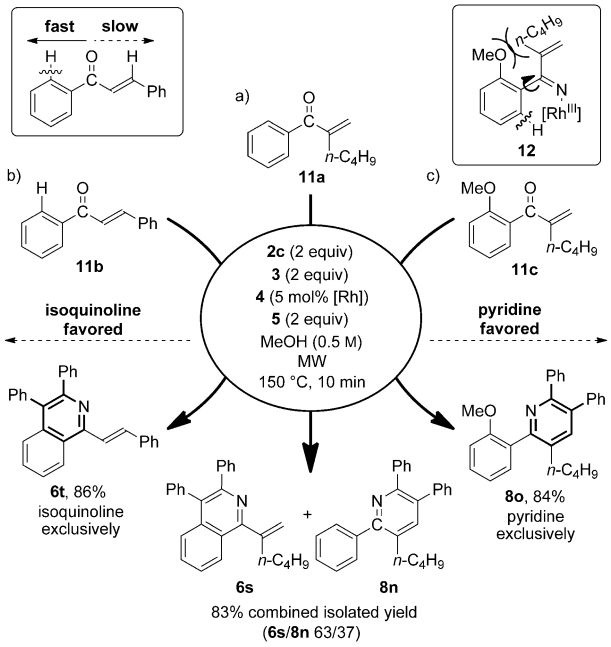
explore this possibility, reaction of 1-(cyclohex-1-en-1-yl)ethanone **7l** with **2a** was performed under the optimized conditions described above. This reaction was found to produce the tetrahydroisoquinoline derivative **8l** along with the unexpected isoquinoline **6e** in a ratio of 77:23 (Scheme 2a). To confirm that **6e** is produced in this process by dehydrogenative oxidation, a mixture of **8l** and the copper catalyst **5** (2 equiv) was heated at 150 °C for 30 min under microwave irradiation conditions. The observation that this reaction generates **6e** (40%) shows that $Cu(OAc)_2$ promotes dehydrogenation of the tetrahydroisoquinoline ring system (Scheme 3). In contrast to that



Scheme 3. Dehydrogenative of **8l** by **5**.

of **7l**, the N-annulation reaction of 1-(cyclopent-1-en-1-yl)ethanone (**7m**) with **2a** is not efficient. It is likely that the β-C–H bond in **7m** is not readily accessible to the metal center, a requirement for C–H bond activation. However, when a greater amount of the Rh catalyst is used, **7m** reacts to form the bicyclic pyridine derivative **8m** in moderate yield (e.g., 5 mol%: 9%; 10 mol%: 58%, Scheme 2b). Finally, 1-acylcycloalkenes containing larger ring systems, such as 1-acetylcycloheptene and 1-acetylcyclooctene, do not undergo the N-annulation reaction.

A notable issue arises in N-annulation reactions of ketones that possess both aryl α,β-unsaturated moieties, in which two C–H bond cleavage sites exist. In these substrates, isoquinolines and pyridines can be generated by activation of the respective *ortho*-C–H and vinyl C–H bonds. To probe this issue, reaction of the aryl α,β-unsaturated ketone **11a** with diphenylacetylene (**2c**) was performed using **3**, **4** (5 mol% [Rh]), and **5** (2 equiv) and microwave irradiation conditions (150 °C). This process generates a mixture of isoquinoline **6s** and pyridine **8n** in a 63:37 ratio and 83% combined yield of isolated products (Scheme 4a). This result suggests that the *ortho* sp^2 C–H bond is more reactive than the vinylic sp^2 C–H bond toward rhodium(III)-catalyzed C–H bond activation.



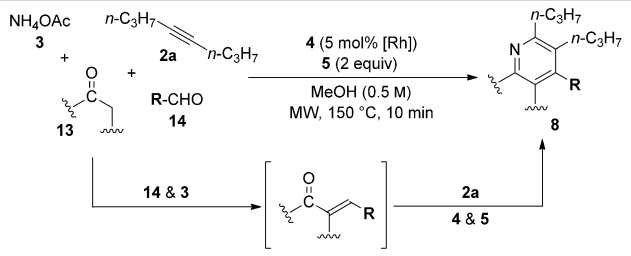
Scheme 4. Chemoselectivity of N-annulation reactions of aryl α,β-enones **11** with **2c** and **3**.

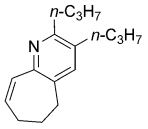
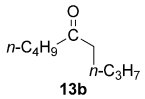
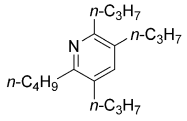
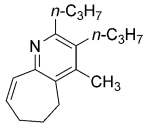
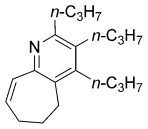
Based on the finding that the bulky β substituents present in α,β-enones retard the N-annulation reaction, we explored the reaction of an aryl α,β-enone, such as chalcone **11b**, that contains a β substituent. Reaction of this substance under the standard conditions was found to result in exclusive formation of isoquinoline **6t** (86% yield of isolated product), thus demonstrating again that the β-phenyl substituent suppresses the pyridine forming process (Scheme 4b). In contrast, N-annulation reaction of aryl α,β-enone **11c**, which bears an *o*-methoxy aryl substituent, leads to production of pyridine **8o** (84%) without competitive formation of an isoquinoline derivative (Scheme 4c). This phenomenon is a likely consequence of the difficulty associated with the Rh-promoted aromatic C–H bond activation step required to form the isoquinoline moiety caused by steric hindrance between the *o*-methoxy group and *n*-butyl group in the key intermediate **12**.

Branched α,β-unsaturated ketones, which serve as substrates for the three-component N-annulation reaction, can be gener-

ated by aldol reactions of alkyl ketones with formaldehyde. Owing to this feature, we anticipated that the overall process involving α,β-unsaturated ketone formation and N-annulation could be carried out in a one-pot manner. The feasibility of this new, four-component N-annulation reaction was explored. The results show that reaction of 2-cycloheptenone (**13a**) with a mixture of paraformaldehyde (**14a**, 1.5 equiv HCHO), **2a**, and **3** in the presence of the catalyst mixture containing **4** (5 mol% [Rh]) and **5** (2 equiv), under microwave irradiation conditions (150 °C), leads to formation of pyridine **8p** isolated in 76% yield (Table 6, entry 1).[10] In addition, reaction of the linear

Table 6. Rh^{III}-catalyzed, four-component N-annulation reaction between ketone **13**, aldehyde **14**, alkyne **2a**, and NH_4OAc (**3**).



Entry	Ketone (**13**)	R–CHO (**14**)	Pyridine (**8**)	Yield [%][a]
1	 **13a**	$(CH_2O)_n$ (**14a**)	 **8p**	76
2	 **13b**	**14a**	 **8q**	50
3	**13a**	CH_3–CHO (**14b**)	 **8r**	10
4	**13a**	n-C_3H_7–CHO (**14c**)		–

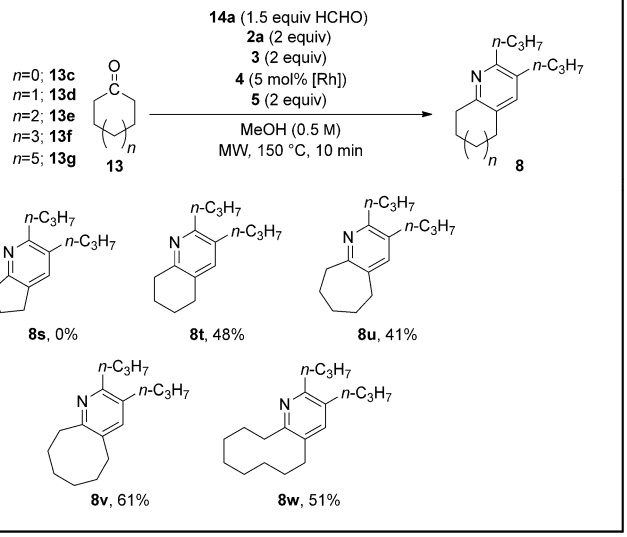
[a] Yield of isolated product.

ketone 5-nonanone (**13b**) with **14a**/**2a**/**3** affords the corresponding pyridine **8q**, which was isolated in 50% yield (Table 6, entry 2).

Studies were conducted to determine if other aldehydes, such as acetaldehyde (**14b**) and butyraldehyde (**14c**), would participate in this four-component N-annulation reaction. The results show that reaction of **13a** with alkyne **2a**, NH_4OAc (**3**), and **14b** gives the corresponding pyridine **8r** in only 10% yield of isolated product (Table 6, entry 3), and that **14c** does not undergo the process (Table 6, entry 4). These observations are consistent with the N-annulation reactivities of α,β-enones that contain β substituents (see above).

The use of cycloalkanones as substrates in this one-pot, four-component N-annulation reaction is interesting because the processes would produce fused pyridines directly. To determine if this process is successful, cyclohexanone (**13d**) was subjected to reaction with alkyne **2a**. This process forms tetrahydroquinoline **8t** in 48% yield of isolated product (Table 7). In

Table 7. Four-component N-annulation reactions of alkyne **2a** with cycloalkanones **13**.



addition we observed that medium-ring-sized cycloalkanones, such as cycloheptanone (**13e**), cyclooctanone (**13f**), and cyclodecanone (**13g**), also undergo reaction with **2a** to afford the corresponding pyridines **8u**, **8v**, and **8w**, which were isolated in moderate yields (41–61%). However, cyclopentanone (**13c**) does not serve as a substrate for this process, a likely consequence of the unfavorable generation of the conformation of the α-methylene ketimine rhodium intermediate required for C–H bond activation.

Conclusion

The investigation described herein has led to the development of a new, microwave-promoted, one-pot N-annulation reaction of aryl and α,β-unsaturated ketones with ammonium acetate and alkynes that produces the respective isoquinoline and pyridine derivatives. The efficiencies of the N-annulation reactions, which are generally high, are lessened by the steric effects of aryl ring and enone substituents. By using this protocol, a variety of isoquinoline and pyridine derivatives were synthesized in high yields. Importantly, the studies have also led to the development of a new one-pot, four-component N-annulation reaction between ketones, formaldehyde, NH_4OAc, and alkynes that generates pyridine derivatives through a pathway initiated by aldol condensation of the ketones with formaldehyde to produce α-methylene ketones.

Experimental Section

General

Flash column chromatography was performed using Merck 230–400 mesh silica gel and column chromatography was monitored by analytical thin-layer chromatography carried out on 0.25 Merck silica gel plates (60F-254) with UV light as a visualizing agent, *p*-anisaldehyde, ninhydrin, and $KMnO_4$ solution as staining solutions, and heat as developing agent. Microwave experiments were performed in a CEM Discover instrument with appropriate internal IR temperature control and 10 mL Pyrex vials. The reaction temperature, pressure, and microwave power were monitored by computer, and a 10 mL thick walled Pyrex vessel with Teflon septa with a crimp top was used as reaction vessel. Gas chromatographic analyses were performed on an Agilent 7890A instrument with flame ionization detector and an Agilent HP-5 capillary column. Mass chromatography analyses were performed on an Agilent 5975C instrument and an Agilent HP-5MS column. IR spectra were recorded using a Bruker Vertex 70 FTIR spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker Advance II/DPX 400 (400 MHz ^1H, 100 MHz ^{13}C) spectrometers with chemical shifts reported relative to residual deuterated solvent peaks. ^1H NMR spectra were referenced to $CDCl_3$ (for ^1H, $\delta = 7.26$ ppm) as internal standard, and are reported as chemical shift multiplicity: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. ^{13}C NMR spectra were referenced to the residual $CDCl_3$ (for ^{13}C, $\delta =$ 77.26 ppm) as internal standard. High-resolution mass spectra were provided by YCRF Yonsei University. Most commercially available reagent-grade chemicals (**1a**–**h**, **1j**–**n**, **2a**–**d**, **3**, **5**, **7a**, **7l**,**m**, **11b**, **13a**–**g**, and **14a**–**c**) were purchased from Aldrich Chemical Company, TCI, and Burdick and Jackson, and used as received without further purification unless otherwise stated. Toluene (purchased from Duksan Chemical) was distilled from sodium/benzophenone under a nitrogen atmosphere prior to use. Complex $[Cp^*RhCl_2]_2$ (**4**)[11] was prepared according to the literature procedure and stored in a refrigerator under a N_2 atmosphere.

Typical procedure for the three component N-annulation reaction (Tables 2–5)

$[Cp^*RhCl_2]_2$ (**4**, 3.1 mg, 0.005 mmol), $Cu(OAc)_2{\cdot}H_2O$ (**5**, 79.9 mg, 0.40 mmol), and NH_4OAc (**3**, 30.8 mg, 0.40 mmol) were added to a MeOH solution (0.1 mL) of 4-methoxyacetophenone (**1a**, 30.0 mg, 0.20 mmol) and 4-octyne (**2a**, 44.1 mg, 0.40 mmol) in 10 mL Pyrex tube. After capping the reaction vessel with Teflon septa, the reaction mixture was stirred at 150 °C for 10 min to ensure homogeneous conditions under microwave irradiation. After cooling to room temperature, the reaction mixture was filtered through a celite pad. The reaction progress was monitored by GC-MS. All volatiles were removed in vacuo, and the resulting crude mixture was subject to flash column chromatography (*n*-hexane/ethyl acetate 20:1) to afford 6-methoxy-1-methyl-3,4-dipropylisoquinoline (**6a**, 48.0 mg, 0.187 mmol) in 93% yield.

6-Methoxy-1-methyl-3,4-dipropylisoquinoline (6a): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.99$ (d, $J = 9.2$ Hz, 1H), 7.18 (d, $J = 2.4$ Hz, 1H), 7.13 (dd, $J = 9.2$, 2.4 Hz, 1H), 3.95 (s, 1H), 2.95–2.86 (m, 7H), 1.80–1.65 (m, 4H), 1.11–1.02 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.5$, 155.2, 152.4, 137.6, 128.2, 125.7, 121.9, 117.4, 102.5, 55.5, 37.7, 30.2, 24.1, 23.9, 22.3, 14.9, 14.6 ppm; IR (CH_2Cl_2): $\tilde{\nu} = 2958$, 2931, 2871, 1715, 1620, 1463, 1414, 1221, 1029, 837 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{17}H_{24}NO^+$ $[M+H]^+$: 258.1852; found: 258.1852.

6-Methoxy-1-methyl-3,4-dipentylisoquinoline (6b): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.91$ (d, $J = 8.8$ Hz, 1H), 7.10 (d, $J = 2.0$ Hz, 1H), 7.05 (dd, $J = 8.8$, 2.4 Hz, 1H), 3.87 (s, 3H), 2.87–2.78 (m, 7H), 1.70–1.53 (m, 4H), 1.45–1.30 (m, 8H), 0.88–0.82 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.4$, 155.2, 152.7, 137.5, 128.2, 125.7, 121.9, 117.4, 102.3, 55.5, 35.9, 32.6, 32.5, 30.7, 30.3, 28.1, 22.9, 22.8, 22.6, 14.4, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu} = 3003$, 2963, 2920, 2856, 1620, 1573, 1464, 1413, 1271, 1129, 1156 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{21}H_{32}NO^+$ $[M+H]^+$: 314.2478; found: 314.2478.

6-Methoxy-1-methyl-3,4-diphenylisoquinoline (6c): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.04$ (d, $J = 9.2$ Hz, 1H), 7.30–7.27 (m, 5H), 7.17–7.12 (m, 6H), 6.91 (d, $J = 2.6$ Hz, 1H), 3.64 (s, 3H), 2.98 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.7$, 157.1, 150.2, 141.3, 138.2, 138.0, 131.4, 130.4, 128.4, 127.7, 127.6, 127.2, 121.8, 118.8, 104.6 ppm.

3-(*tert*-Butyl)-6-methoxy-1,4-dimethylisoquinoline (6d): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.95$ (d, $J = 9.2$ Hz, 1H), 7.19 (d, $J = 2.0$ Hz, 1H), 7.12 (dd, $J = 9.2$, 2.4 Hz, 1H), 3.94 (s, 1H), 2.84 (s, 3H), 2.70 (s, 3H), 1.53 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.1$, 158.1, 153.1, 139.3, 127.8, 121.3, 120.9, 117.8, 101.9, 55.5, 38.6, 31.2, 22.8, 16.5 ppm; IR (CH_2Cl_2): $\tilde{\nu} = 3049$, 2954, 2871, 1620, 1579, 1505, 1413, 1362, 1272, 1230, 1045 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{22}NO^+$ $[M+H]^+$: 244.1696; found: 244.1696.

1-Methyl-3,4-dipropylisoquinoline (6e): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 8.0$ Hz, 1H), 7.94 (d, $J = 9.2$ Hz, 1H), 7.64 (t, $J =$ 7.2 Hz, 1H), 7.47 (t, $J = 7.2$ Hz, 1H), 2.99–2.91 (m, 7H), 1.83–1.76 (m, 2H), 1.71–1.62 (m, 2H), 1.10–1.03 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 155.8$, 151.4, 135.6, 129.8, 126.7, 126.3, 125.6, 123.7, 37.1, 29.9, 24.3, 24.0, 21.9, 14.7, 14.5 ppm.

1-Methyl-3,4-dipropyl-6-(trifluoromethyl)isoquinoline (6f): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.24$ (s, 1H), 8.18 (d, $J = 8.8$ Hz, 1H), 7.66 (dd, $J = 8.8$, 1.6 Hz, 1H), 3.01 (t, $J = 8.0$ Hz, 2H), 2.95–2.91 (m, 5H), 1.85–1.75 (m, 2H), 1.72–1.63 (m, 2H), 1.10 (t, $J = 7.2$ Hz, 3H), 1.05 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 156.0$, 153.6, 134.9, 131.6, 131.3, 131.0, 130.7, 127.6, 127.1, 125.7, 123.0, 121.6, 121.5, 121.5, 121.4, 121.2, 121.1, 121.1, 121.1, 37.7, 29.9, 24.6, 23.9, 22.7, 14.7, 14.6 ppm; IR (CH_2Cl_2): $\tilde{\nu} = 2962$, 2933, 2874, 1573, 1446, 1338, 1307, 1160, 1130, 1090, 822 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{17}H_{21}F_3N^+$ $[M+H]^+$: 296.1621; found: 296.1621.

6-Pentyl-2,3-dipropylpyridine (6g): ^1H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.10 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H), 7.61 (t, $J = 8.0$ Hz, 1H), 7.46 (t, $J = 7.6$ Hz, 1H), 3.24 (t, $J = 7.6$ Hz, 2H), 2.99–2.90 (m, 4H), 1.87–1.75 (m, 4H), 1.72–1.62 (m, 2H), 1.49–1.33 (m, 4H), 1.10–1.02 (m, 6H), 0.90 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.7$, 151.8, 136.0, 129.4, 126.2, 126.0, 125.5, 125.3, 123.9, 37.5, 35.7, 32.3, 30.1, 30.0, 24.3, 23.9, 22.8, 14.8, 14.5, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu} = 3071$, 2958, 2930, 2871, 1697, 1566, 1461, 1338, 1257, 1088, 759 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{20}H_{30}N^+$ $[M+H]^+$: 284.2373; found: 284.2373.

1-Phenyl-3,4-dipropylisoquinoline (6h): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.00$ (d, $J = 7.6$ Hz, 2H), 7.65–7.59 (m, 3H), 7.48–7.35 (m, 4H), 3.07–3.00 (m, 4H), 1.89–1.83 (m, 2H), 1.76–1.70 (m, 2H), 1.14–1.03 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 158.3$, 152.4, 140.3, 136.3, 130.2, 129.6, 128.4, 128.3, 128.2, 127.3, 125.5, 125.4, 123.5, 37.6, 30.1, 24.3, 23.8, 14.9, 14.5 ppm.

1-Cyclohexyl-3,4-dipropylisoquinoline (6i): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.16$ (d, $J = 8.4$ Hz, 1H), 7.94 (d, $J = 8.4$ Hz, 1H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.43 (t, $J = 7.6$ Hz, 1H), 3.50–3.45 (m, 1H), 2.97–2.88 (m, 4H), 1.94–1.77 (m, 9H), 1.70–1.61 (m, 2H), 1.55–1.46 (m, 2H), 1.42–1.35 (m, 1H), 1.08 (t, $J = 7.2$ Hz, 3H), 1.01 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 162.4$, 151.7, 135.9, 129.0, 125.5, 125.2, 125.0, 124.8, 124.0, 41.6, 37.4, 32.8, 30.1, 27.2, 26.6,

24.3, 23.3, 14.9, 14.5 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3071, 2957, 2928, 2870, 2853, 1565, 1450, 1336, 1263, 1088, 985 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{21}H_{30}N^+$ $[M+H]^+$: 296.2373; found: 296.2361.

2,3-Dipropyl-8,9-dihydro-7*H*-benzo[*de*]quinolone (6j): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 6.8 Hz, 1H), 3.20 (t, *J* = 6.0 Hz, 2H), 3.07 (t, *J* = 6.0 Hz, 2H), 2.97–2.88 (m, 4H), 2.19–2.12 (m, 2H), 1.83–1.73 (m, 2H), 1.71–1.62 (m, 2H), 1.10–1.03 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 151.8, 139.2, 135.9, 129.6, 126.2, 123.9, 123.7, 121.1, 37.7, 34.7, 31.0, 30.2, 24.3, 24.1, 23.6, 14.8, 14.6 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2957, 2870, 2835, 1609, 1571, 1390, 1330, 1255, 1091, 791 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{18}H_{24}N^+$ $[M+H]^+$: 254.1903; found: 254.1901.

1,7-Dimethyl-3,4-dipropylisoquinoline (6k): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.82 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 1H), 2.95 (t, *J* = 8.0 Hz, 2H), 2.90–2.87 (m, 5H), 2.52 (s, 3H), 1.83–1.73 (m, 2H), 1.70–1.61 (m, 2H), 1.09–1.02 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1, 151.0, 135.0, 133.8, 131.7, 126.4, 126.2, 125.2, 123.7, 37.6, 30.0, 24.5, 24.0, 22.6, 21.9, 14.8, 14.6 ppm.

***N*-(1-Methyl-3,4-dipropylisoquinolin-7-yl)acetamide (6l)**: M.p. 140–144 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.3 (s, 1H), 7.90 (d, *J* = 8.8 Hz, 1H), 7.72 (d, *J* = 6.8 Hz, 2H), 2.96–2.85 (m, 7H), 2.24 (s, 3H), 1.81–1.72 (m, 2H), 1.69–1.59 (m, 2H), 1.09–1.01 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 155.4, 151.2, 135.2, 132.8, 126.6, 126.4, 124.9, 123.6, 115.1, 37.5, 30.0, 24.9, 24.5, 24.1, 22.6, 14.8, 14.6 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2958, 2929, 2870, 1723, 1669, 1624, 1583, 1550, 1320, 1276, 875, 829 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{18}H_{25}N_2O^+$ $[M+H]^+$: 285.1961; found: 285.1956.

1-Methyl-3,4-dipropylisoquinolin-7-amine (6m): M.p. 185–191 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.8 Hz, 1H), 7.17 (d, *J* = 2.0 Hz, 1H), 7.10 (dd, *J* = 9.2, 2.4 Hz, 1H), 3.92 (s, 2H), 2.93–2.89 (m, 2H), 2.86–2.82 (m, 2H), 2.79 (s, 3H), 1.80–1.71 (m, 2H), 1.69–1.59 (m, 2H), 1.09–1.01 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 148.8, 143.7, 129.8, 127.6, 126.4, 125.3, 121.6, 107.0, 37.4, 30.1, 24.6, 24.2, 22.6, 14.9, 14.6 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3341, 3183, 2958, 2929, 2869, 1641, 1624, 1566, 1511, 1414, 1242, 856, 830 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{23}N_2^+$ $[M+H]^+$: 243.1856; found: 243.1847.

1-Methyl-3,4-dipropylisoquinolin-7-ol (6n): M.p. 175–181 °C; ^1H NMR (400 MHz, CD_2Cl_2): δ = 12.68 (s, 1H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.34 (d, *J* = 9.2 Hz, 1H), 2.92–2.82 (m, 4H), 2.71 (s, 3H), 1.73–1.68 (m, 2H), 1.58–1.53 (m, 2H), 1.04–0.96 ppm (m, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 157.7, 153.5, 144.6, 131.0, 130.1, 128.1, 126.1, 125.9, 108.2, 34.7, 30.1, 24.8, 24.6, 19.4, 14.8, 14.5 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3355, 2958, 2924, 2852, 1670, 1585, 1451, 1361, 1289, 884, 787, 686 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{22}NO^+$ $[M+H]^+$: 244.1696; found: 244.1696.

7-Methoxy-1-methyl-3,4-diphenylisoquinoline (6o): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 9.2 Hz, 1H), 7.38–7.30 (m, 6H), 7.25–7.14 (m, 6H), 7.97 (s, 3H), 3.03 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 156.2, 148.0, 141.3, 138.0, 131.6, 130.5, 129.4, 128.4, 128.2, 127.8, 127.5, 127.3, 126.9, 122.4, 103.7, 55.7, 23.1 ppm.

5-Methoxy-1-methyl-3,4-diphenylisoquinoline (6p): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.23–7.21 (m, 2H), 7.16–7.09 (m, 8H), 6.95 (d, *J* = 7.6 Hz, 1H), 3.40 (s, 3H), 3.04 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 157.1, 151.4, 141.9, 141.7, 130.6, 130.5, 128.2, 128.0, 127.7, 127.5, 127.3, 126.7, 125.9, 118.3, 110.3, 55.8, 23.6 ppm.

7-Methyl-4,5-dipropylthieno[2,3-*c*]pyridine (6q): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 5.2 Hz, 1H), 7.38 (d, *J* = 5.2 Hz, 1H), 2.91–2.84 (m, 4H), 2.74 (s, 3H), 1.81–1.73 (m, 2H), 1.71–1.61 (m, 2H), 1.05–1.01 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.3, 149.6, 145.6, 133.3, 130.5, 126.9, 122.7, 36.8, 32.0, 24.5, 24.3, 23.6, 14.7, 14.6 ppm.

7-Methyl-4,5-dipropylfuro[2,3-*c*]pyridine (6r): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 2.0 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 2.84–2.77 (m, 4H), 2.70 (s, 3H), 1.77–1.60 (m, 4H), 1.03–0.98 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 149.5, 147.1, 139.5, 134.1, 125.7, 105.5, 36.7, 31.8, 24.4, 24.3, 18.6, 14.5 ppm.

1-(Hex-1-en-2-yl)-3,4-diphenylisoquinoline (6s): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.4 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.40–7.33 (m, 5H), 7.28–7.26 (m, 2H), 7.21–7.16 (m, 3H), 5.64 (s, 1H), 5.32 (s, 1H), 2.80 (t, *J* = 7.4 Hz, 2H), 1.65–1.53 (m, 2H), 1.49–1.42 (m, 2H), 0.93 ppm (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9, 149.3, 148.1, 141.2, 137.9, 137.1, 131.6, 130.7, 130.6, 130.1, 129.5, 128.5, 127.7, 127.4, 127.2, 126.5, 126.1, 125.6, 117.2, 37.1, 30.3, 22.8, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3058, 3027, 2956, 2869, 2858, 1542, 1501, 1445, 1378, 766, 698 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{26}N^+$ $[M+H]^+$: 364.2060; found: 364.2045.

3,4-Diphenyl-1-styrylisoquinoline (6t): ^1H NMR (400 MHz, $CDCl_3$): δ = 8.43 (d, *J* = 8.0 Hz, 1H), 8.16–8.06 (m, 2H), 7.72–7.68 (m, 2H), 7.61–7.54 (m, 2H), 7.48–7.46 (m, 2H), 7.42–7.30 (m, 6H), 7.26–7.19 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 150.1, 141.4, 138.0, 137.4, 137.0, 136.3, 131.6, 130.8, 130.1, 130.0, 129.0, 128.7, 128.5, 127.8, 127.7, 127.5, 127.3, 126.9, 126.5, 125.6, 124.5, 123.2 ppm.

1-Cyclohexylprop-2-en-1-one (7b): ^1H NMR (400 MHz, $CDCl_3$): δ = 6.43 (dd, *J* = 17.6, 10.4 Hz, 1H), 6.25 (d, *J* = 17.2 Hz, 1H), 5.75 (d, *J* = 10.4 Hz, 1H), 2.65–2.58 (m, 1H), 1.85–1.68 (m, 5H), 1.42–1.26 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.8, 135.2, 128.0, 48.4, 28.8, 26.1, 25.9 ppm.

1,1-Diphenylbut-3-en-2-one (7c): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.21 (m, 10H), 6.47 (dd, *J* = 17.2, 10.0 Hz, 1H), 6.34 (dd, *J* = 17.6, 1.6 Hz, 1H), 5.73 (dd, *J* = 10.0, 1.2 Hz, 1H), 5.33 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.8, 138.4, 135.6, 129.4, 129.2, 128.9, 127.5, 62.5 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3085, 3061, 3029, 1716, 1657, 1598, 1494, 1449, 1317, 1278, 747, 701 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{14}ONa^+$ $[M+Na]^+$: 245.0937; found: 245.0932.

4-Methylene-1-phenylheptan-3-one (7d): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.17 (m, 5H), 5.96 (s, 1H), 5.69 (s, 1H), 3.02–2.91 (m, 4H), 2.25 (t, *J* = 7.6 Hz, 2H), 1.47–1.37 (m, 2H), 0.90 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3, 141.6, 128.7, 128.6, 126.3, 124.0, 39.8, 33.1, 30.6, 21.8, 14.0 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3028, 2960, 2872, 1718, 1678, 1603, 1453, 1273, 1069, 936 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{14}H_{19}O^+$ $[M+H]^+$: 203.1430; found: 203.1422.

4-Methylene-1-phenylnonan-3-one (7e): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.16 (m, 5H), 5.95 (s, 1H), 5.69 (s, 1H), 3.02–2.90 (t, *J* = 7.2 Hz, 6H), 1.42–1.25 (m, 6H), 0.88 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.2, 149.3, 141.6, 128.7, 128.6, 126.3, 123.8, 39.8, 31.8, 31.1, 30.6, 28.4, 22.7, 14.2 ppm; IR (CH_2Cl_2): 3063, 3028, 2956, 2858, 1711, 1678, 1454, 1410, 1077, 932 cm^{-1}; HRMS (EI+): *m/z* calcd for $C_{16}H_{22}O^+$ $[M]^+$: 230.1671; found: 230.1675.

4-Methylene-1-phenyldodecanonan-3-one (7f): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.26 (m, 2H), 7.21–7.17 (m, 3H), 5.96 (s, 1H), 5.70 (s,1H), 3.03–2.99 (m, 2H), 2.95–2.91 (m, 2H), 2.26 (t, *J* = 7.1 Hz, 2H), 1.40–1.36 (m, 2H), 1.32–1.24 (m, 5H), 0.88 ppm (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3, 149.3, 141.6, 128.7, 128.6, 126.3, 123.8, 39.9, 32.1, 31.2, 30.7, 29.7, 29.6, 29.5, 28.7, 22.9, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3086, 3062, 3027, 2954, 2926, 2854, 1679, 1495, 1454, 1265, 748, 699 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{19}H_{28}ONa^+$ $[M+Na]^+$: 295.2032; found: 295.2019.

4-Methylene-1-phenyltetradecanonan-3-one (7g): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.19 (m, 5H), 5.95 (s, 1H), 5.69 (s, 1H), 3.02–2.91 (m, 4H), 2.26 (t, J = 6.8 Hz, 2H), 1.30–1.26 (m, 18H), 0.88 ppm (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.2, 149.3, 141.6, 128.7, 128.6, 126.3, 123.8, 39.9, 32.1, 31.1, 30.6, 29.8, 29.7, 29.6, 29.6, 28.7, 22.9, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3063, 3028, 2925, 2854, 1711, 1681, 1496, 1455, 1282, 1077 cm^{-1}; HRMS (EI+): m/z calcd for $C_{21}H_{32}O^+$ $[M]^+$: 300.2453; found: 300.2456.

5-Phenylpent-1-en-3-one (7h): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.26 (m, 3H), 7.21–7.17 (m, 3H), 6.36 (dd, J = 17.6, 10.4 Hz, 1H), 5.83 (dd, J = 10.4, 0.8 Hz, 1H), 2.97–2.90 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.9, 141.3, 136.7, 128.6, 128.5, 128.4, 126.3, 41.4, 30.0 ppm.

1-Phenylhex-4-en-3-one (7i): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.24 (m, 2H), 7.22–7.15 (m, 3H), 6.88–6.82 (m, 1H), 6.13 (dd, J = 1.56, 15.8 Hz, 1H), 2.96–2.92 (m, 2H), 2.88–2.84 (m, 2H), 1.89 ppm (dd, J = 1.56, 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.5, 143.0, 141.5, 132.1, 128.6, 128.5, 126.2, 41.7, 30.2, 18.5 ppm.

1-Phenyloct-4-en-3-one (7j): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.18 (m, 5H), 6.84–6.76 (m, 1H), 2.94–2.83 (m, 4H), 2.19–2.13 (m, 2H), 1.51–1.44 (m, 2H), 0.97 ppm (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.6, 147.6, 141.4, 130.6, 128.6, 128.5, 126.2, 41.7, 34.6, 30.2, 21.5, 13.8 ppm.

6,6-Dimethyl-1-phenylhept-4-en-3-one (7k): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.26 (m, 2H), 7.21–7.18 (m, 3H), 6.79 (d, J = 16.0 Hz, 1H), 6.00 (d, J = 16.0 Hz, 1H), 2.96–2.85 (m, 4H), 1.06 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.3, 157.4, 141.5, 128.7, 128.6, 126.2, 125.6, 42.0, 33.9, 30.3, 28.9 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3062, 2961, 2905, 2867, 1696, 1673, 1495, 1454, 1364, 1296, 983 cm^{-1}; HRMS (ESI): m/z calcd for $C_{15}H_{20}ONa^+$ $[M+Na]^+$: 239.1406; found: 239.1406.

6-Pentyl-2,3-dipropylpyridine (8a): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (d, J = 7.7 Hz, 1H), 6.88 (d, J = 7.7 Hz, 1H), 2.75–2.68 (m, 4H), 2.54 (t, J = 7.6 Hz, 2H), 1.74–1.54 (m, 6H), 1.34–1.31 (m, 4H), 0.98 (q, J = 7.2 Hz, 6H), 0.86 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 159.4, 137.2, 132.2, 120.0, 38.4, 37.3, 34.2, 31.9, 30.2, 24.2, 23.6, 22.8, 14.5, 14.3, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2958, 2929, 2871, 1737, 1591, 1571, 1463, 1377, 1242, 829 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{28}N^+$ $[M+H]^+$: 234.2216; found: 234.2208.

6-Cyclohexyl-2,3-dipropylpyridine (8b): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.0 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 2.73 (t, J = 8.0 Hz, 2H), 2.67–2.63 (m, 1H), 2.54 (t, J = 7.6 Hz, 2H), 1.96–1.94 (m, 2H), 1.83–1.82 (m, 2H), 1.74–1.67 (m, 4H), 1.64–1.55 (m, 2H), 1.49–1.36 (m, 4H), 1.01–0.96 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 159.3, 137.2, 132.3, 117.6, 46.4, 37.3, 34.2, 33.4, 26.9, 26.5, 24.1, 23.4, 14.5, 14.4 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3054, 2958, 2927, 2853, 1589, 1570, 1459, 1400, 1377, 1132, 830, 740 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{28}N^+$ $[M+H]^+$: 246.2216; found: 246.2211.

6-Benzhydryl-2,3-dipropylpyridine (8c): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.25 (m, 6H), 7.20–7.17 (m, 5H), 6.81 (d, J = 7.6 Hz, 1H), 5.62 (s, 1H), 2.74 (t, J = 7.6 Hz, 2H), 2.55 (t, J = 7.6 Hz, 2H), 1.72–1.66 (m, 2H), 1.64–1.56 (m, 2H), 0.99–0.92 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 159.5, 143.8, 137.1, 133.0, 130.3, 129.7, 128.5, 128.4, 126.4, 121.2, 59.3, 37.1, 34.2, 24.0, 23.0, 14.4, 14.4 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3060, 3026, 2960, 2930, 2870, 1586, 1571, 1494, 1452, 1078, 1031, 748, 699 cm^{-1}; HRMS (ESI): m/z calcd for $C_{24}H_{28}N^+$ $[M+H]^+$: 330.2216; found: 330.2204.

2-Phenethyl-3,5,6-tripropylpyridine (8d): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.17 (m, 5H), 7.16 (s, 1H), 3.08–3.00 (m, 4H), 2.77 (t, J = 7.6 Hz, 2H), 2.55 (t, J = 7.6 Hz, 2H), 2.46 (t, J = 7.6 Hz, 2H), 1.79–1.69 (m, 2H), 1.65–1.48 (m, 4H), 1.03–0.91 ppm (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.7, 142.7, 138.0, 132.6, 132.5, 128.7, 128.5, 126.0, 36.8, 36.5, 36.2, 34.2, 34.1, 24.2, 24.1, 23.4, 14.5, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2959, 2930, 2871, 1732, 1453, 1266, 1110, 748, 708 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{32}N^+$ $[M+H]^+$: 310.2529; found: 310.2514.

3-Pentyl-2-phenethyl-5,6-dipropylpyridine (8e): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.15 (m, 5H), 7.13 (s, 1H), 3.07–2.98 (m, 2H), 2.74 (t, J = 8.8 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 2.46 (t, J = 8.0 Hz, 2H), 1.76–1.69 (m, 2H), 1.65–1.55 (m, 2H), 1.53–1.45 (m, 2H), 1.35–1.26 (m, 6H), 1.03–0.96 (m, 6H), 0.89 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 155.6, 142.6, 138.1, 132.8, 132.7, 128.7, 128.5, 126.0, 36.6, 36.4, 36.2, 34.1, 32.0, 32.0, 30.7, 24.2, 23.5, 22.7, 14.5, 14.3, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3027, 2958, 2870, 1712, 1452, 1237, 1075, 749 cm^{-1}; HRMS (ESI): m/z calcd for $C_{24}H_{36}N^+$ $[M+H]^+$: 338.2842; found: 338.2842.

3-Octyl-2-phenethyl-5,6-dipropylpyridine (8f): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.11 (m, 5H), 3.09–3.00 (m, 4H), 2.73 (t, J = 7.7 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 2.46 (t, J = 7.6 Hz, 2H), 1.78–1.69 (m, 2H), 1.65–1.55 (m, 2H), 1.50–1.46 (m, 2H), 1.35–1.23 (m, 5H), 1.03–0.96 (m, 6H), 0.88 ppm (t, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.7, 142.8, 138.0, 132.7, 132.7, 132.7, 128.8, 128.5, 126.0, 36.8, 36.6, 36.2, 34.2, 32.1, 32.0, 31.0, 29.9, 29.7, 29.5, 24.2, 23.5, 22.9, 14.5, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3026, 2957, 2926, 2856, 1591, 1576, 1494, 1452, 748, 698 cm^{-1}; HRMS (ESI): m/z calcd for $C_{27}H_{42}N^+$ $[M+H]^+$: 380.3312; found: 380.3296.

3-Decyl-2-phenethyl-5,6-dipropylpyridine (8g): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.17 (m, 5H), 7.11 (s, 1H), 3.01 (br s, 4H), 2.72 (t, J = 7.6 Hz, 2H), 2.53 (t, J = 7.4 Hz, 2H), 2.45 (t, J = 7.5 Hz, 2H), 1.75–1.70 (m, 2H), 1.68–1.57 (m, 2H), 1.48 (m, 2H), 1.30–1.21 (m, 14H), 1.02–0.95 (m, 6H), 0.87 ppm (t, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.7, 142.7, 138.0, 132.7, 132.6, 128.8, 128.7, 128.6, 128.5, 126.0, 36.8, 36.6, 36.2, 34.1, 32.1, 32.0, 31.8, 31.0, 29.8, 29.7, 29.6, 24.2, 23.5, 22.93, 22.91, 14.5, 14.4 ppm.

6-Phenethyl-2,3-dipropylpyridine (8h): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.24 (m, 3H), 7.20–7.15 (m, 3H), 6.84 (d, J = 7.8 Hz, 2H), 3.09–3.01 (m, 4H), 2.78 (t, J = 7.8 Hz, 2H), 2.57 (t, J = 7.6 Hz, 2H), 1.79–1.69 (m, 2H), 1.65–1.56 (m, 2H), 1.05–0.97 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 158.0, 142.1, 137.4, 132.7, 128.7, 128.5, 126.0, 120.4, 39.8, 37.1, 36.4, 34.1, 29.9, 24.1, 23.5, 14.5, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3084, 3061, 3027, 2959, 2929, 2870, 1716, 1590, 1573, 1495, 1455, 749, 698 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{26}N^+$ $[M+H]^+$: 268.2060; found: 268.2047.

4-Methyl-6-phenethyl-2,3-dipropylpyridine (8i): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.24 (m, 3H), 7.21–7.15 (m, 2H), 6.73 (s, 1H), 3.04–2.98 (m, 4H), 2.77 (t, J = 8.0 Hz, 2H), 2.57 (t, J = 8.4 Hz, 2H), 2.25 (s, 3H), 1.78–1.68 (m, 2H), 1.55–1.45 (m, 2H), 1.04–1.00 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 153.6, 139.3, 132.4, 130.0, 128.8, 128.6, 128.0, 126.3, 37.6, 35.1, 31.3, 24.0, 23.7, 22.7, 15.8, 14.8, 14.7 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3061, 3027, 2959, 2930, 2871, 1714, 1603, 1565, 1494, 1453, 727, 698 cm^{-1}; HRMS (ESI): m/z calcd for $C_{20}H_{27}N^+$ $[M+H]^+$: 282.2216; found: 282.2201.

1-Methyl-3,4-dipropyl-5,6,7,8-tetrahydroisoquinoline (8l): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.70–2.67 (m, 4H), 2.58 (t, J = 8.4 Hz, 2H), 2.51 (t, J = 8.4 Hz, 2H), 2.37 (s, 3H), 1.77–1.65 (m, 6H), 1.49–1.44 (m, 2H), 1.03–0.98 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 153.5, 144.2, 131.1, 128.3, 37.4, 30.3, 26.7, 24.1, 23.5, 22.8, 22.7, 22.2, 14.9, 14.7 ppm.

1-Methyl-3,4-dipropyl-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine (8m): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.85 (q, J = 8.0 Hz, 4H), 2.71 (t, J = 8.0 Hz, 2H), 2.53 (t, J = 8.0 Hz, 2H), 2.40 (s, 3H), 2.10–2.03 (m, 2H), 1.73–1.67 (m, 2H), 1.52–1.46 (m, 2H), 1.02–0.97 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 152.8, 150.3, 135.5, 129.2, 37.0, 32.0, 31.9, 31.1, 24.6, 24.3, 23.7, 22.0, 14.7, 14.6 ppm; IR

(CH_2Cl_2): $\tilde{\nu}$ = 2959, 2932, 2870, 1712, 1584, 1459, 1431, 1234, 1091 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{15}H_{24}N^+$ $[M+H]^+$: 218.1903; found: 218.1901.

3-Butyl-2,5,6-triphenylpyridine (8n): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.60 (m, 3H), 7.48–7.38 (m, 5H), 7.32–7.20 (m, 6H), 2.74 (t, *J* = 7.7 Hz, 2H), 1.62–1.55 (m, 2H), 1.37–1.29 (m, 2H), 0.86 ppm (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 154.2, 140.2, 134.7, 134.4, 130.3, 129.9, 129.5, 128.5, 128.3, 128.1, 128.0, 127.8, 127.7, 127.3, 33.5, 32.0, 22.8, 14.1 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3059, 3028, 2956, 2928, 2859, 1551, 1495, 1446, 1426, 1378, 766, 699 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{26}N^+$ $[M+H]^+$: 364.2060; found: 364.2045.

3-Butyl-2-(2-methoxyphenyl)-5,6-diphenylpyridine (8o): M.p. 133–137 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.60 (s, 1H), 7.39–7.35 (m, 4H), 7.28–7.22 (m, 5H), 7.19–7.17 (m, 3H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.80 (s, 3H), 2.56–2.52 (m, 2H), 1.55–1.47 (m, 2H), 1.29–1.20 (m, 2H), 0.80 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.6, 154.2, 140.6, 140.5, 139.0, 135.9, 134.7, 131.5, 130.4, 130.2, 129.9, 129.6, 128.4, 127.9, 127.5, 127.2, 121.0, 111.0, 55.7, 32.7, 31.7, 22.8, 14.1 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2956, 2928, 2858, 2835, 1600, 1580, 1491, 1459, 1424, 1025, 752, 699 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{28}NO^+$ $[M+H]^+$: 394.2165; found: 394.2167.

Typical procedure for the four-component N-annulation reaction (Table 6)

A 10 mL Pyrex tube was charged with 2-cycloheptenone (**13a**, 22.0 mg, 0.20 mmol), 4-octyne (**2a**, 44.1 mg, 0.40 mmol), paraformaldehyde (**14a**, 9.0 mg, 0.30 mmol), $[Cp^*RhCl_2]_2$ (**4**, 3.1 mg, 0.005 mmol), $Cu(OAc)_2{\cdot}H_2O$ (**5**, 80.0 mg, 0.40 mmol), NH_4OAc (**3**, 30.8 mg, 0.40 mmol), and MeOH (0.1 mL), and the reaction vessel was capped with Teflon septa. The reaction was performed with internal magnetic stirring for 10 min to ensure homogeneous conditions at 150 °C under microwave irradiation. After cooling to room temperature, the reaction mixture was filtered through a celite pad. The reaction progress was monitored by GC-MS. Then, all volatiles were removed in vacuo and the resulting crude mixture was subject to flash column chromatography (*n*-hexane/ethyl acetate 20:1) to give 2,3-dipropyl-6,7-dihydro-5*H*-cyclohepta[*b*]pyridine (**8p**, 34.8 mg, 0.152 mmol) in 76% yield.

2,3-Dipropyl-6,7-dihydro-5*H*-cyclohepta[*b*]pyridine (8p): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.15 (s, 1H), 6.25 (dt, *J* = 12.3, 1.9 Hz, 1H), 5.93–5.89 (m, 1H), 3.04 (t, *J* = 5.2 Hz, 2H), 2.72–2.68 (m, 2H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.46 (m, 2H), 2.00–1.94 (m, 2H), 1.74–1.64 (m, 2H), 1.64–1.54 (m, 2H), 1.01–0.95 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 157.0, 139.4, 133.2, 132.6, 128.9, 127.5, 38.8, 36.9, 33.9, 32.8, 25.1, 24.2, 23.6, 14.6, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2959, 2929, 2870, 1736, 1551, 1452, 1246, 1065, 921 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{24}N^+$ $[M+H]^+$: 230.1903; found: 230.1895.

2-Butyl-3,5,6-tripropylpyridine (8q): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.11 (s, 1H), 2.71 (q, *J* = 8.0 Hz, 4H), 2.52 (t, *J* = 7.6 Hz, 4H), 1.72–1.54 (m, 8H), 1.46–1.36 (m, 2H), 1.00–0.92 ppm (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 156.9, 137.9, 132.2, 132.2, 36.9, 34.7, 34.2, 32.6, 24.3, 23.6, 23.2, 14.5, 14.4, 14.4 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2959, 2931, 2871, 1688, 1451, 1339, 1091, 921 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{18}H_{32}N^+$ $[M+H]^+$: 262.2529; found: 262.2519.

4-Methyl-2,3-dipropyl-6,7-dihydro-5*H*-cyclohepta[*b*]pyridine (8r): ^1H NMR (400 MHz, $CDCl_3$): δ = 6.53 (d, *J* = 11.6 Hz, 1H), 6.16–6.10 (m, 1H), 2.83 (t, *J* = 6.4 Hz, 2H), 2.74–2.70 (m, 2H), 2.61–2.57 (m, 2H), 2.26–2.17 (m, 5H), 2.14–2.08 (m, 2H), 1.75–1.65 (m, 2H), 1.54–1.43 (m, 2H), 1.05–1.00 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.7, 157.3, 143.3, 132.9, 131.6, 129.1, 126.9, 38.1, 36.9, 31.2, 31.2, 28.8, 24.0, 23.8, 15.7, 14.8, 14.7 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 3022, 2958, 2927, 2870, 1702, 1554, 1454, 1415, 1377, 1091, 804, 722 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{17}H_{26}N^+$ $[M+H]^+$: 244.2060; found: 244.2052.

2,3-Dipropyl-5,6,7,8-tetrahydroquinoline (8t): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.08 (s, 1H), 2.86 (t, *J* = 6.0 Hz, 2H), 2.70 (t, *J* = 8.0 Hz, 4H), 2.52 (t, *J* = 7.6 Hz, 2H), 1.88–1.84 (m, 2H), 1.80–1.74 (m, 2H), 1.70–1.63 (m, 2H), 1.63–1.56 (m, 2H), 1.02–0.96 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 154.0, 137.8, 132.4, 129.4, 37.2, 34.1, 32.3, 28.6, 24.3, 23.9, 23.6, 23.1, 14.6, 14.4 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2958, 2932, 2870, 1737, 1690, 1563, 1450, 1188, 927 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{15}H_{24}N^+$ $[M+H]^+$: 218.1903; found: 218.1903.

2,3-Dipropyl-6,7,8,9-tetrahydro-5*H*-cyclohepta[*b*]pyridine (8u): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.09 (s, 1H), 2.97 (t, *J* = 5.6 Hz, 2H), 2.71–2.67 (m, 4H), 2.52 (t, *J* = 7.6 Hz, 2H), 1.85–1.81 (m, 2H), 1.74–1.54 (m, 8H), 1.01–0.96 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 156.3, 137.8, 135.2, 132.3, 39.2, 36.9, 35.1, 34.0, 32.8, 28.4, 27.0, 24.3, 23.7, 14.6, 14.4 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2958, 2924, 2870, 1703, 1562, 1454, 1338, 1164, 960 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{26}N^+$ $[M+H]^+$: 232.2060; found: 232.2056.

2,3-Dipropyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (8v): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.09 (s, 1H), 2.90 (t, *J* = 6.4 Hz, 2H), 2.74–2.68 (m, 4H), 2.54 (t, *J* = 7.6 Hz, 2H), 1.76–1.57 (m, 8H), 1.36–1.35 (m, 4H), 1.00–0.95 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.7, 157.5, 137.7, 133.2, 132.7, 37.1, 34.4, 34.1, 32.5, 31.7, 31.0, 26.3, 26.2, 24.2, 23.9, 14.5, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$ = 2957, 2927, 2869, 1561, 1451, 1360, 1171, 1088, 919 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{17}H_{28}N^+$ $[M+H]^+$: 246.2216; found: 246.2206.

2,3-Dipropyl-5,6,7,8,9,10,11,12-octahydrocyclodeca[*b*]pyridine (8w): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.14 (s, 1H), 2.92 (t, *J* = 6.0 Hz, 2H), 2.78 (t, *J* = 6.8 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H), 2.54 (t, *J* = 7.6 Hz, 2H), 1.95–1.89 (m, 2H), 1.80–1.75 (m, 2H), 1.74–1.66 (m, 2H), 1.65–1.55 (m, 2H), 1.49–1.46 (m, 4H), 1.14–1.07 (m, 4H), 0.99–0.95 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 156.6, 137.4, 132.4, 132.3, 36.8, 34.1, 31.1, 29.4, 28.7, 28.6, 26.8, 26.5, 24.2, 23.5, 21.1, 20.7, 14.3, 14.3 ppm; IR (CH_2Cl_2): $\tilde{\nu}$2996, 2928, 2869, 1706, 1595, 1555, 1447, 838, 705 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{19}H_{32}N^+$ $[M+H]^+$: 274.2529; found: 274.2517.

2-Methylene-1-phenylhexan-1-one (11a): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.8 Hz, 2H), 7.55–7.48 (m, 3H), 5.80 (s, 1H), 5.56 (s, 1H), 2.47 (t, *J* = 10.8 Hz, 2H), 1.50–1.42 (m, 6H), 0.92 ppm (t, *J* = 11.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.2, 149.3, 141.6, 128.7, 128.6, 126.3, 123.8, 39.8, 31.8, 31.1, 30.6, 28.4, 22.7, 14.2 ppm.

1-(2-Methoxyphenyl)-2-methylenehexan-1-one (11c): ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 1.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.97–6.90 (m, 2H), 5.80 (s, 1H), 5.59 (s, 1H), 3.75 (s, 3H), 2.44 (t, *J* = 7.2 Hz, 2H), 1.54–1.46 (m, 2H), 1.43–1.36 (m, 2H), 0.94 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 157.2, 150.0, 131.4, 129.7, 129.2, 127.8, 120.4, 111.6, 55.8, 30.6, 30.5, 22.6, 14.2 ppm.

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