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An Approach to Five-Membered Lactams from Aliphatic Amides and Terminal Acetylenes by Nickel Catalysis

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Abstract: A nickel-catalyzed facile synthesis of structurally diverse five-membered lactams from aliphatic amides and terminal acetylenes with the assistance of an 8-aminoquinolyl auxiliary has been achieved. A broad range of terminal acetylenes and aliphatic amides proved to be the efficient coupling partners, furnishing the corresponding lactams in moderate to good yields. The transformation is proven to undergo an oxidative alkynylation followed by the intramolecular annulation process. The methodology can be extended to aromatic amides and acrylamides, which provides an efficient and straightforward protocol for the construction of a variety of isoindolinone and pyrrolidinone derivatives.

Keywords: alkynylation/intramolecular annulations; C–H activation; isoindolinone derivatives; lactams; nickel

Introduction

Transition-metal-catalyzed direct functionalization of inert C–H bonds has aroused more and more attention for the efficient construction of structurally diverse heterocycles in a step- and atom-economical manner.[1] Among various useful heterocyclic compounds, the lactam moiety is the privileged structural motif in terms of many complex natural products and pharmaceutical compounds with a broad range of biological activities.[2] Over the past few years, many pioneering works for the efficient synthesis of lactam derivatives have been well explored,[3] and the strategy for facile preparation of lactams though direct C(sp^2)–H bond functionalization has been well applied in organic synthesis. In contrast, protocols involving the direct functionalization of sp^3 C–H bonds are limited. The first example for the construction of five-membered lactam compounds through the functionalization of unactivated C(sp^3)–H bonds was reported by Yu and co-workers, in which the palladium-catalyzed oxidative coupling of aliphatic amides with electron-deficient alkenes and sequential Michael addition resulted in the lactam compounds.[4] The palladium-catalyzed intramolecular amination of unactivated C(sp^3)–H bonds for the construction of five-membered lactam compounds was reported by Chen and co-workers.[5] Later, the rapid synthesis of four-membered lactams through the intramolecular amination of unactivated C(sp^3)–H bonds was successfully developed by Shi,[6] Kanai[7] and Ge[8] independently by using different transition metal catalysts. Very recently, the precious metal-catalyzed tandem carbonylation of unactivated C(sp^3)–H bonds and sequential intramolecular amination was demonstrated by the group of Chatani,[9] Yu,[10] Gaunt[11] and Wang.[12] We recently reported a cobalt-catalyzed cyclization of terminal alkynes and aliphatic amides for the synthesis of five-membered lactams.[18] Despite these significant progresses, the development of alternative and promising catalysts for lactams is highly desired. In this paper, we report a new approach to the five-membered lactams through nickel-catalyzed alkynylation of C(sp^3)–H bonds and consecutive annulation from aliphatic amides and terminal alkynes.

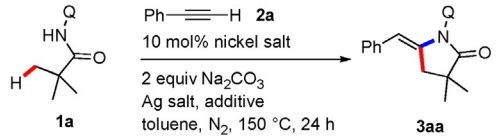
Nickel is a less expensive and more sustainable transition metal. While the intrinsic properties of nickel catalyst enable many useful transformations that are even not achievable with palladium catalysts, the application of nickel catalysts in C-H fuctionalizations is in its early stage. Recently, landmark results by using nickel catalysts in a variety of C-H activation

reactions were successfully realized by Chatani and others.[13] Due to the great significance and challenge of inert C(sp^3)–H functionalization, much attention has been turned towards the nickel catalyzed C(sp^3)–H transformations, and many important transformations, including arylation,[14] alkylation,[15] and intramolecular amidation[8] have been achieved. We recently developed the nickel-catalyzed C–S bond formation from unactivated sp^3 C–H bonds.[16a] Inspired by the above encouraging achievements and our continuous endeavour of catalytic functionalization of sp^3 C–H bonds,[16,17] we explored the possibility of the diverse lactam skeleton construction from unactivated C(sp^3)–H bonds by nickel catalysis.

Results and Discussion

At the outset of the study, we examined the reaction between *N*-(quinolin-8-yl)pivalamide **1a** and phenylacetylene **2a** in the presence of 10 mol% $NiBr_2$ catalyst and Ag_2CO_3 oxidant in toluene at 150 °C under N_2 atmosphere. However, no desired product was observed (Table 1, entry 1). To our delight, the desired lactam product **3a** was isolated in 63% yield when TBAI was added in the reaction (Table 1, entry 2). Encouraged by this satisfying result, we next screened

Table 1. Optimization of the reaction conditions[a]



Entry	[Ni]	Ag salt	Additive	Yield (%)[b]
1	$NiBr_2$	Ag_2CO_3	–	0
2	$NiBr_2$	Ag_2CO_3	TBAI	63
3	$NiCl_2$	Ag_2CO_3	TBAI	75 (6:1)[c]
4	NiI_2	Ag_2CO_3	TBAI	79
5	**$(Cy_3P)_2NiCl_2$**	**Ag_2CO_3**	**TBAI**	**91**
6	$(Ph_3P)_2NiCl_2$	Ag_2CO_3	TBAI	85
7	$Ni(OAc)_2$	Ag_2CO_3	TBAI	71 (4:1)[c]
8	–	Ag_2CO_3	TBAI	0
9	$(Cy_3P)_2NiCl_2$	Ag_2O	TBAI	42
10	$(Cy_3P)_2NiCl_2$	AgOAc	TBAI	trace
11	$(Cy_3P)_2NiCl_2$	AgI	TBAI	trace
12	$(Cy_3P)_2NiCl_2$	Ag_2CO_3	ZnI_2	0
13	$(Cy_3P)_2NiCl_2$	Ag_2CO_3	NaI	trace
14	$(Cy_3P)_2NiCl_2$	Ag_2CO_3	KI	trace
15	$(Cy_3P)_2NiCl_2$	–	TBAI	0

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Cat. Ni (0.01 mmol), Na_2CO_3 (0.2 mmol), Ag salt (0.4 mmol) and additive (0.3 mmol), toluene (1.5 mL) in N_2 at 150 °C for 24 h.

[b] Isolated yield, Q = 8-quinolinyl.

[c] The ratio of *E*- and *Z*-isomer products, determined by ^{1}H NMR, is in parentheses.

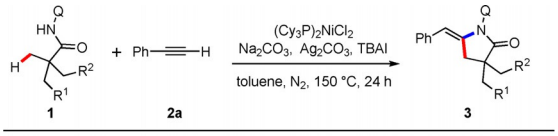
other nickel catalysts, including $NiCl_2$, NiI_2, $(Cy_3P)_2NiCl_2$, $(Ph_3P)_2NiCl_2$ and $Ni(OAc)_2$ (Table 1, entries 3–7). It was found that $(Cy_3P)_2NiCl_2$ showed the best catalytic reactivity and gave the lactam product in 91% yield (Table 1, entry 5). No reaction occurred in the absence of nickel catalyst (Table 1, entry 8). The effect of a range of different silver salts and additives was also tested in the reaction (Table 1, entries 9–11 and 12–14), and the best result was obtained by using Ag_2CO_3 oxidant in combination with TBAI (Table 1, entry 5). No product was observed when the reaction performed without the Ag_2CO_3 (Table 1, entry 15). Further optimization of solvents revealed that toluene was superior and the coordinating solvents such as DMF and DMSO had a detrimental effect on the reaction (See Supporting Information). Meanwhile, the reaction could perform smoothly in a number of common solvents, including PhF, $PhCF_3$ and xylene, delivering the desired product in satisfactory yields (See Supporting Information).

With the optimized reaction conditions in hand, the compatibility and applicability of this nickel-catalyzed protocol were investigated. We first examined the scope of different aliphatic amide substrates and the results were shown in Table 2. To our delight, a wide range of aliphatic amides were subjected to the standard conditions and afforded the relevant lactam products in moderate to excellent yields with exclusive *E*-configuration (Table 2, **3a–l**). The different substituents at the α-carbon of the aliphatic amides led to the formation of two racemic pairs of enantiomers, which were generated by the chiral C3 and the axial chirality of the lactam ring (Table 2, **3b–l**). Notably, the reaction exhibited high regioselectivity and the sp^3 C–H activation exclusively occurred at the β-methyl group instead of the β-methylene and γ-methyl groups.

It was worth mentioning that α-cyclic amides could smoothly participate in the reaction to give the corresponding spiral lactam products with good yields (Table 2, **3m–o**).

Encouraged by the feasibility of the current nickel-catalyzed tandem reaction using various aliphatic amides as coupling partners, we turned to investigate the reactivity of a series of terminal alkynes. As shown in Table 3, a wide range of terminal alkynes are compatible with the reaction system and the corresponding functionalized lactam products were obtained in moderate to good yields. The reactivity of *ortho*- and *meta*-substituted phenylacetylene was dramatically lower than *para*-substituted phenylacetylene, revealing that the steric hindrance exerted obvious influence on the reaction (**4a–c**). Aryl acetylenes with electron-withdrawing substituents, such as F, Cl and Br, showed similar reactivity compared with electron-rich aryl acetylene, which was suggestive of the negligible electron effect on the transformation (**4d–**

Table 2. The scope of various aliphatic amides react with **2a**[a,b]



Entry	Substrate	Product	Yield (%)	d.r.
1	**1a**	**3a**	91	–
2	**1b**	**3b**	94	1.1:1
3	**1c**	**3c**	93	1.1:1
4	**1d**	**3d**	93	1.1:1
5	**1e**	**3e**	74	2:1
6	**1f**	**3f**	68	2:1
7	**1g**	**3g**	56	1.1:1
8	**1h**	**3h**	73	1.7:1
9	**1i**	**3i**	70	1:1.2
10	**1j**	**3j**	95	1:1.1
11	**1k**	**3k**	62	1.1:1
12	**1l**	**3l**	81	1.2:1
13	**1m**	**3m**	57	–
14	**1n**	**3n**	68	–
15	**1o**	**3o**	81	–

g). The arylation products were not detected by either the TLC and GC-MS when we studied the reaction of *N*-(quinolin-8-yl)pivalamide (**1a**) with 1-bromo-4-ethynylbenzene (**2h**) under standard reaction conditions. Gratifyingly, some heterocyclic alkynes, including thiophenyl group, could participate in the reaction, giving the lactam products **4h–4i** but in relatively lower yields. It should be noted that the aliphatic alkynes were applicable under the standard conditions as well, affording the desired product in acceptable yields (**4j–l**, 45–56%). However, neither alkynylation product nor lactam (**4m**) was observed when the reaction was performed with ethynyltriisopropylsilane (**2n**). The structure and configuration of lactam product **4e** was unambiguously confirmed by single-crystal X-ray diffraction analysis (Figure 1).[19]

Isoindolinones are important heterocycles due to their unique biological properties and wide applications in pharmaceutical chemistry and material science. Therefore, the reactivity of aromatic amides was investigated to further extend the protocol for the synthesis of isoindolinones. It was found that a wide variety of benzamides successfully reacted with phenylacetylene (**2a**) under the reaction conditions to give the corresponding isoindolinone products in moderate to excellent yields (Table 4). Both electron-rich and electron-deficient benzamides readily reacted irrespective of the electron nature of the substituents in the aryl ring (**6a–j**). 1-Naphthalenecarboxamide proved to be a viable substrate for the reaction, which gave a mixture of *Z*- and *E*-isomeric products **6k** in 86% isolated yield. It was found that the transformation proceeded well with some heterocyclic amides and moderate reactivity was observed (**6l–m**).

A variety of aryl acetylenes were subjected to the reaction to further examine the applicability of the transformation (Table 5), and the corresponding isoindolinones were obtained in high yields (**7a–n**). The structure of the product **7f** was further confirmed by single-crystal X-ray diffraction analysis (Figure 2).[19] Heterocyclic and aliphatic acetylenes participated in the reaction well to afford the desired isoindolinones with moderate to high yields (**7i–n**).

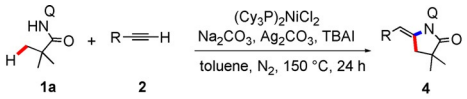
It is noteworthy that the reaction of acrylamides proceeded smoothly without a significant decrease in the yield to give the pyrrolidinones (Table 6), which are useful intermediates of bioactive products and functional materials (**9a–c**).

To gain insights into the reaction mechanism, we performed some control experiments (Scheme 1). The

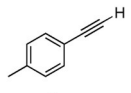
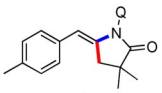
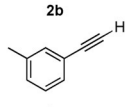
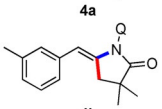
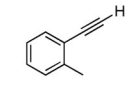
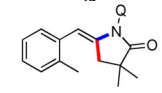
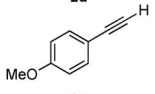
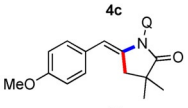
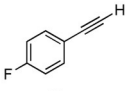
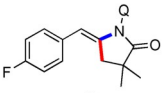
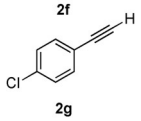
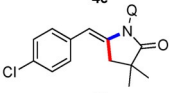
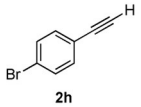
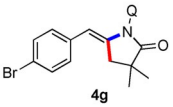
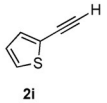
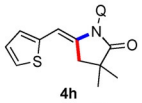
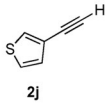
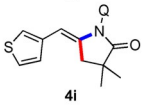
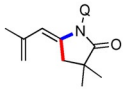
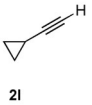
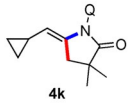
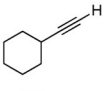
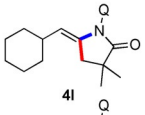
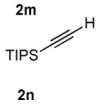
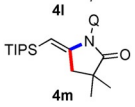
[a] Reaction conditions: **1** (0.1 mmol), phenylacetylene **2a** (0.3 mmol), Cat. Ni (0.01 mmol), Na_2CO_3 (0.2 mmol), Ag salt (0.4 mmol) and additive (0.3 mmol), toluene (1.5 mL) in N_2 at 150 °C for 24 h.

[b] Isolated yield, the ratio of two isomer products, determined by ^1H NMR, is in parentheses.

Table 3. The scope of various terminal alkynes reacting with **1a**[a,b]

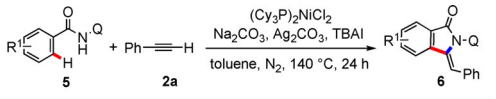


1a 2 4

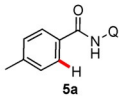
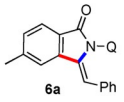
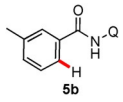
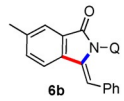
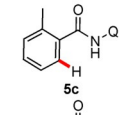
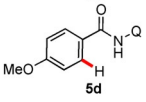
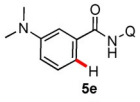
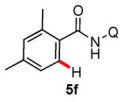
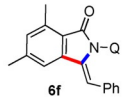
Entry	Substrate	Product	Yield (%)
1	 2b	 4a	83
2	 2c	 4b	74
3	 2d	 4c	62
4	 2e	 4d	62
5	 2f	 4e	71
6	 2g	 4f	62
7	 2h	 4g	53
8	 2i	 4h	42
9	 2j	 4i	44
10	 2k	 4j	45
11	 2l	 4k	55
12	 2m	 4l	56
13	 2n	 4m	0

[a] Reaction conditions: **1a** (0.1 mmol), phenylacetylene **2** (0.3 mmol), Cat. Ni (0.01 mmol), Na_2CO_3 (0.2 mmol), Ag salt (0.4 mmol) and additive (0.3 mmol), toluene (1.5 mL) in N_2 at 150 °C for 24 h.
[b] Isolated yield. Q = 8-quinolinyl.

Table 4. The scope of various aromatic amides reacting with **2a**[a,b]



5 2a 6

Entry	Substrate	Product	Yield (%)
1	 5a	 6a	80
2	 5b	 6b	61
3	 5c	 6c	45
4	 5d	 6d	75
5	 5e	 6e	57
6	 5f	 6f	81
7	5g	6g	71
8	5h	6h	71
9	5i	6i	52
10	5j	6j	61
11	5k	6k	86 Z/E=2:1
12	5l	6l	45
13	5m	6m	54

[a] Reaction conditions: **5** (0.1 mmol), phenylacetylene **2a** (0.3 mmol), Cat. Ni (0.01 mmol), Na_2CO_3 (0.2 mmol), Ag salt (0.4 mmol) and additive (0.3 mmol), toluene (1.5 mL) in N_2 at 140 °C for 24 h.
[b] Isolated yield.
[c] The ratio of Z- and E-isomer products was presented in parentheses and determined by ^1H NMR.

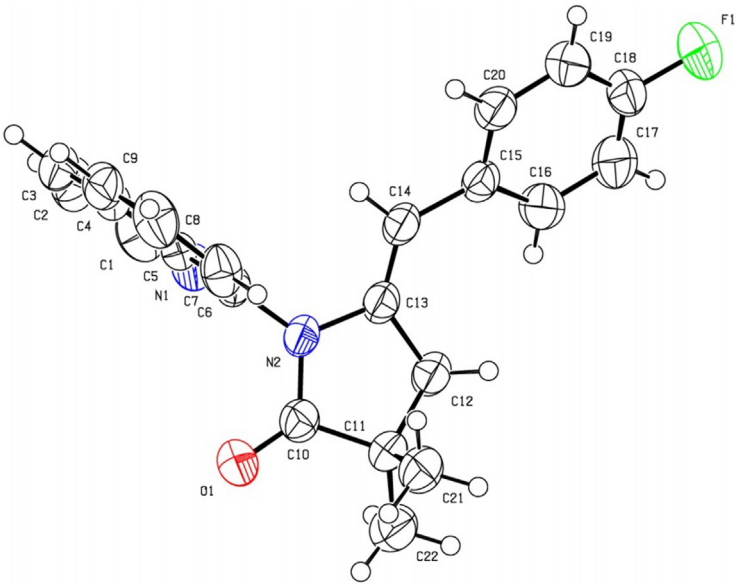


Figure 1. X-Ray Structure of **4e**

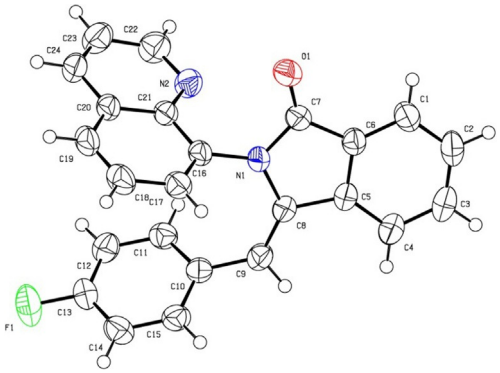


Figure 2. X-Ray Structure of **7f**

addition of a radical scavenger such as TEMPO (2,2,6,6-Tetramethylpiperidine 1-oxyl) or BHT (2,4-di-tert-butyl-4-methylPhen-ol) into the reaction hardly influenced the reaction, implying that a radical process may not be involved in the reaction process (Scheme 1, eq 1). This phenomenon is quite different with the cobalt-catalyzed cyclization of aliphatic amides and acetylenes.[18] GC-MS analysis of the reaction solution for 5 h revealed that alkynylated product was produced, which is consistent with a reaction pathway of first alkynylation and then cyclization (Scheme 1, eq 2 and eq 3). Based on these experimental results and previous reports, a tentative reaction mechanism is proposed as shown in Scheme 2. First, the cyclometalation of Ni^{II} generates intermediate **A** with the assistance of 8-aminoquinaline auxiliary. The subsequent oxidation of Ni^{II} to Ni^{III} and ligand exchange forms the intermediate **B**, which undergoes the reductive elimination to give the alkynylated product **10**. The result of MALDI-TOF analysis supports the possible formation of intermediate **B** (see Supporting Information). The oxidation of Ni^{I} generates the Ni^{II} species through protonation to end the cycle. We prepared the intermediate **10** by a literature method[20] and studied the cyclization reaction. It was found that the silver salt in combination with TBAI promoted the cyclization rapidly (Scheme 1, eq 4).

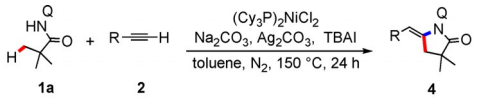
Conclusions

In summary, we have developed a highly efficient method for direct synthesis of diverse lactam and isoindolinone derivatives from aliphatic/aryl amides and terminal acetylenes by nickel catalysis, which provides a new approach for the rapid assembly of these useful heterocycles. The acrylamides can also be reacted smoothly under the same condition, giving pyrrolidinones in moderate yields. A general reaction mechanism has been proposed involving formation of the intermediate **B**, which has been identified by MALDI-TOF. Further studies to explore other novel transition-metal-catalyzed reactions are now in progress.

Experimental Section

General Information. All reactions were performed under N_2 atmosphere in a 25 mL sealed tube. Toluene was dried and distilled according to the standard procedures before the use. Other materials and solvents were purchased from common commercial sources and used without additional purification. Starting materials were synthesized according to literature procedures. ^{1}H NMR spectra were recorded at 400 MHz using TMS as internal standard, ^{13}C NMR spectra

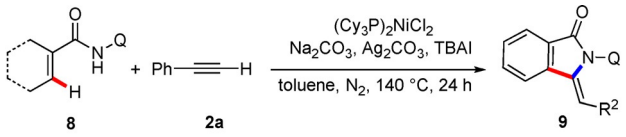
Table 5. The scope of various terminal alkynes reacting with **5m**[a,b]



1a 2 4

Entry	Substrate	Product	Yield (%)
1	2a	7a	84
2	2b	7b	89
3	2c	7c	86
4	2d	7d	81
5	2e	7e	92
6	2f	7f	81
7	2g	7g	74
8	2h	7h	83
9	2i	7i	76
10	2j	7j	86
11	2k	7k	65
12	2l	7l	46
13	2m	7m	82
14	2n	7n	71

Table 6. The scope of various acrylamides reacting with **2a**[a,b]



8 2a 9

Entry	Substrate	Product	Yield (%)
1	8a	9a	57
2	8b	9b	65
3	8c	9c	62

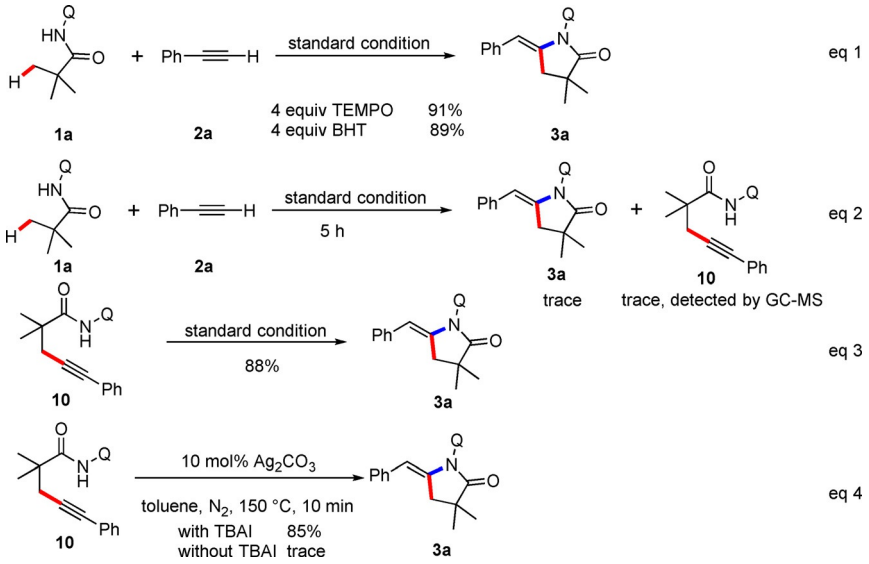
[a] Reaction conditions: **8** (0.1 mmol), phenylacetylene **2a** (0.3 mmol), Cat. Ni (0.01 mmol), Na_2CO_3 (0.2 mmol), Ag salt (0.4 mmol) and additive (0.3 mmol), 1,3,5-Trimethylbenzene (1.5 mL) in N_2 at 130 °C for 24 h.
[b] Isolated yield. Q = 8-quinolinyl.

were recorded at 100 MHz using TMS as internal standard. The multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), multiplet (m), triplet (t) and broad resonances (br). Mass spectroscopy data of the products were collected on an HRMS-TOF instrument.

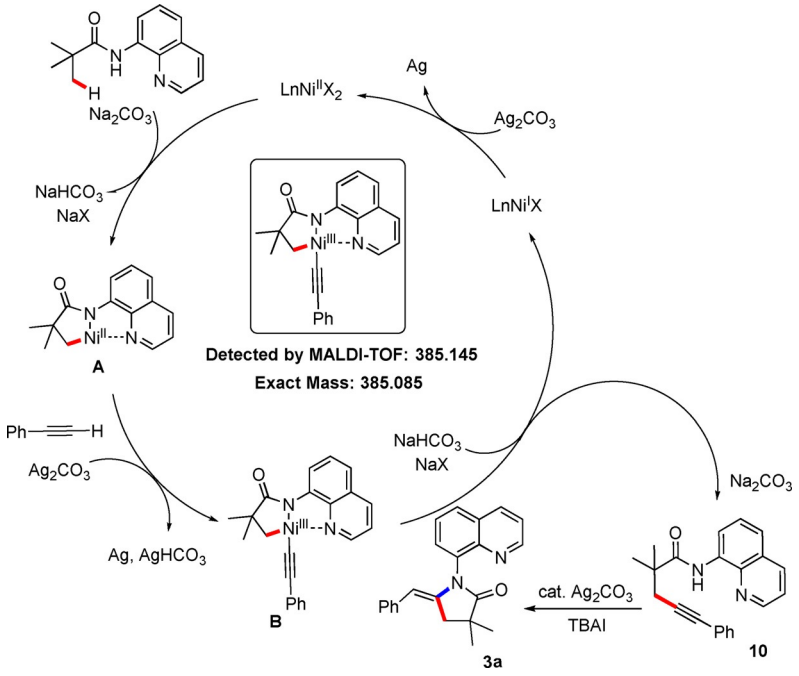
Preparation of 2,2-dimethyl-5-phenyl-*N*-(quinolin-8-yl)pent-4-ynamide (10) according to literature procedures.[20]

To a solution of freshly prepared LDA (39 mmol) in THF (35 mL) cooled to −78 °C was added a solution of ethyl isobutyrate (5.0 mL, 37 mmol) in THF (42 mL) by addition funnel over 1 h with stirring. After addition was completed, the reaction mixture stirred for 20 min at −78 °C and then warmed to 0 °C and stirred for 10 min before cooling back to −78 °C. A solution of propargyl bromide (5.0 mL, 80 wt% in toluene, 45 mmol) in THF (21 mL) was then added dropwise. The mixture was stirred overnight and warmed to room temperature. After quenching with NH_4Cl (aq. ~60 mL) the organic layer was separated and the aqueous layer extracted with Et_2O (2×20 mL). The organic layers were combined and washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated to a brown oil. This oil was purified by flash column chromatography on silica gel, eluting with hexane, to afford ethyl 2,2-dimethyl-4-pen-

[a] Reaction conditions: **1a** (0.1 mmol), phenylacetylene **2** (0.3 mmol), Cat. Ni (0.01 mmol), Na_2CO_3 (0.2 mmol), Ag salt (0.4 mmol) and additive (0.3 mmol), toluene (1.5 mL) in N_2 at 150 °C for 24 h.
[b] Isolated yield. Q = 8-quinolinyl.



Scheme 1. Control Experiments



Scheme 2. Plausible Mechanism

tynoate. Then ethyl 2,2-dimethyl-4-pentynoate (4.63 g, 30 mmol) was added to a solution of dry, degassed triethylamine/acetonitrile (100 mL, 1:4, 0.3 M) and iodobenzene (6.71 mL, 60 mmol). After stirring at room temperature for 10 min, $Pd(PPh_3)_4$ (243 mg, 0.21 mmol, 0.7 mol%) and CuI (286 mg, 1.5 mmol, 5 mol%) were added. The reaction mixture was stirred at room temperature in the dark for 22 h. The crude mixture was then filtered through a plug of Celite and concentrated to a yellow oil. The oil was purified by flash chromatography, eluting with hexane, to afford the product as a colorless oil. Then, to a solution of NaOH (1.77 g, 44 mmol) in methanol/H_2O (2:1, 205 mL, 0.1 M) was added the ethyl 2,2-dimethyl-5-phenyl-4-pentynoate (5.11 g, 22 mmol). The mixture was heated at reflux (80 °C) for 4 h. After cooling back to room temperature, the crude mixture was concentrated and then diluted with H_2O (15 mL). The aqueous mixture was extracted with Et_2O (3×10 mL). The aqueous layer was acidified to pH 2 with concentrated HCl and extracted with ethyl acetate (3×20 mL). These extracts were washed with brine (~10 mL), dried over $MgSO_4$ and concentrated to white solid. Oxalyl chloride (1.8 mL, 20 mmol) was added slowly to a stirred solution of the 2,2-dimethyl-5-phenyl-4-pentynoic acid in CH_2Cl_2 (20 mL) and DMF (0.1 mL) at 0 °C. The mixture was stirred for 1 h at

0 °C and another 4 h at room temperature, and evaporated in vacuo. The residue was then dissolved in toluene (5 mL), evaporated in vacuo twice, to give the crude acid chloride, which was used directly for the next step without further purification. The acid chloride was added dropwise to a solution of 8-aminoquinoline (1.01 g, 7.0 mmol) and Et_3N (1.7 mL, 12 mmol) in CH_2Cl_2 (12 mL). The mixture was stirred overnight at room temperature. Then the mixture was diluted with CH_2Cl_2 (10 mL), washed successively with water, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:20, v/v), to afford 2,2-dimethyl-5-phenyl-*N*-(quinolin-8-yl)pent-4-ynamide (**10**) as a white solid. 2.25 g. Yield: 98%. Melting point: 70.3–72.5 °C (EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H), 8.83 (d, J = 7.6 Hz, 1H), 8.66 (dd, J_1 = 1.6 Hz, J_2 = 2.8 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.47–7.55 (m, 2H), 7.37–7.41 (m, 1H), 7.32–7.34 (m, 2H), 7.17–7.23 (m, 3H), 2.85 (s, 2H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 148.3, 138.8, 136.3, 134.6, 131.7, 128.1, 127.9, 127.7, 127.4, 123.7, 121.6, 121.5, 116.4, 86.8, 83.5, 43.8, 31.1, 25.2. HRMS (EI-TOF) calcd for $C_{22}H_{20}N_2O$ (M^+): 328.1576, found 328.1576.

General procedure for the nickel-catalyzed annulation of aliphatic amides 1 with terminal alkynes 2 (Table 2 and 3).

A 25 mL sealed tube was charged with 2,2-disubstituted *N*-(quinolin-8-yl)propionamide (0.1 mmol), acetylene (0.3 mmol), $(Cy_3P)_2NiCl_2$ (6.9 mg, 0.01 mmol), Na_2CO_3 (21.2 mg, 0.2 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol), TBAI (110.8 mg, 0.3 mmol) and toluene (1.5 mL). The vial was evacuated and filled with N_2 atmosphere, and stirred at 150 °C for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc (2 mL), filtered through a Celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:5~1:2, v/v), to afford the desired alkylated product.

(*E*)-5-Benzylidene-3,3-dimethyl-1-(quinolin-8 yl)-pyrrolidin-2-one (3a). 29.86 mg. Yield, 91%. R_f 0.51 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.18 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.91 (dd, J_1 = 1.6 Hz; J_2 = 7.6 Hz, 1H), 7.62–7.70 (m, 2H), 7.40 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.21–7.24 (m, 2H), 7.06–7.10 (m, *3*H), 5.28 (s, 1H), 3.26 (dd, J_1 = 1.6 Hz; J_2 = 16.0 Hz, 1H), 3.12 (dd, J_1 = 2.0 Hz; J_2 = 16.0 Hz, 1H), 1.53 (s, 3H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 151.2, 144.3, 143.0, 137.0, 136.2, 133.4, 130.4, 129.6, 129.3, 128.3, 127.6, 126.4, 125.2, 121.9, 104.4, 41.2, 40.9, 26.1, 25.7. HRMS (EI-TOF) calcd for $C_{22}H_{20}N_2O$ (M^+): 328.1576, found: 328.1574.

(*Z*)-5-Benzylidene-3,3-dimethyl-1-(quinolin-8-yl-)pyrrolidin-2-one (3a′). 4.59 mg. Yield, 14% (entry 7, Table 1). R_f 0.53 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ([D_6]DMSO, 400 MHz) δ 8.86 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 8.17 (dd, J_1 = 1.6 Hz; J_2 = 8.0 Hz, 1H), 7.67 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.45 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 7.37 (dd, J_1 = 1.2 Hz; J_2 = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 6.58 (t, J = 7.2 Hz, 1H), 6.44 (t, J = 7.6 Hz, 2H), 6.36 (d, J = 7.2 Hz, 2H), 5.69 (s, 1H), 2.88–2.96 (m, 2H), 1.39 (s, 3H), 1.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 150.1, 143.2, 138.6, 135.9, 134.6, 134.2, 129.2, 128.3, 128.0, 127.7, 125.9, 125.5, 124.7, 121.4, 102.7, 42.7, 39.9, 25.0, 24.5. HRMS (EI-TOF) calcd for $C_{22}H_{20}N_2O$ (M^+): 328.1576, found: 328.1574.

(*E*)-5-Benzylidene-3-ethyl-3-methyl-1-(quinolin-8-yl)pyrrolidin-2-one (3b). 32.16 mg. Yield, 94%. The ratio of two isomers was 1.1:1 as determined by ^{1}H NMR. Rf_1 = 0.53, Rf_2 = 0.59 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.87 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.85 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.20 (t, J = 2.0 Hz, 1H), 8.18 (t, J = 2.0 Hz, 1H), 7.92–7.93 (m, 1H), 7.90–7.91 (m, 1H), 7.62–7.69 (m, 4H), 7.41 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 7.39 (dd, J_1 = 2.4 Hz; J_2 = 4.0 Hz, 1H), 7.21–7.25 (m, 5H), 7.06–7.12 (m, 5H), 5.27 (s, 1H), 5.25 (s, 1H), 3.33 (dd, J_1 = 2.0 Hz; J_2 = 16.4 Hz, 1H), 3.21 (dd, J_1 = 2.0 Hz; J_2 = 16.0 Hz, 1H), 3.14 (dd, J_1 = 2.0 Hz; J_2 = 16.4 Hz, 1H), 3.00 (dd, J_1 = 2.0 Hz; J_2 = 16.4 Hz, 1H), 1.69–1.95 (m, 4H), 1.51 (s, 3H), 1.40 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H), 1.05 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.7, 180.6, 151.2, 151.0, 144.3, 143.4, 143.3, 137.1, 136.2, 136.1, 133.5, 133.4, 130.5, 130.4, 129.6, 129.6, 129.3, 129.2, 128.3, 127.6, 126.4, 126.4, 125.2, 121.9, 104.2, 103.9, 44.6, 38.1, 38.1, 31.7, 31.4, 24.5, 24.0, 9.0, 8.9. HRMS (EI-TOF) calcd for $C_{23}H_{22}N_2O$ (M^+): 342.1732, found: 342.1731.

(*E*)-5-Benzylidene-3-methyl-3-propyl-1-(quinolin-8-yl)pyrrolidin-2-one (3c). 31.87 mg. Yield, 93%. The ratio of two isomers was 1.1:1 as determined by ^{1}H NMR. Rf_1 = 0.52, Rf_2 = 0.55 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.88 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.86 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.21 (t, J = 2.0 Hz, 1H), 8.19 (t, J = 2.0 Hz, 1H), 7.93–7.94 (m, 1H), 7.91–7.92 (m, 1H), 7.63–7.69 (m, 4H), 7.42 (dd, J_1 = 2.8 Hz; J_2 = 4.4 Hz, 1H), 7.40 (dd, J_1 = 2.8 Hz; J_2 = 4.0 Hz, 1H), 7.21–7.25 (m, 4H), 7.06–7.12 (m, 6H), 5.27 (s, 1H), 5.24 (s, 1H), 2.98–3.36 (m, 4H), 1.70–1.98 (m, 8H), 1.51 (s, 3H), 1.40 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H), 1.06 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.6, 179.5, 150.1, 150.0, 143.3, 142.3, 142.2, 136.0, 135.1, 135.0, 132.5, 132.3, 129.4, 129.3, 128.5, 128.5, 128.2, 128.1, 127.3, 126.5, 125.3, 125.3, 124.1, 120.8, 103.1, 102.9, 43.6, 43.6, 37.1, 37.0, 30.6, 30.4, 21.7, 21.6, 18.4, 17.8, 13.3, 13.1. HRMS (EI-TOF) calcd for $C_{23}H_{22}N_2O$ (M^+): 342.1732, found: 342.1731.

(*E*)-5-Benzylidene-3-butyl-3-methyl-1-(quinolin-8-yl)pyrrolidin-2-one (3d). 34.42 mg. Yield, 93%. The ratio of two isomers was 1.1:1 as determined by ^{1}H NMR. Rf_1 = 0.54, Rf_2 = 0.55 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.85–8.88 (m, 2H), 8.21 (t, J = 1.6 Hz, 1H), 8.18 (t, J = 1.6 Hz, 1H), 7.90–7.93 (m, 2H), 7.65–7.68 (m, 4H), 7.39–7.43 (m, 2H), 7.21–7.25 (m, 4H), 7.06–7.12 (m, 6H), 5.27 (s, 1H), 5.24 (s, 1H), 3.00–3.36 (m, 4H), 1.76–1.86 (m, 4H), 1.52 (s, 3H), 1.41 (s, 3H), 1.26–1.35 (m, 8H), 0.93–0.99 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.8, 180.7, 151.2, 151.0, 144.3, 143.4, 143.3, 137.1, 136.1, 136.1, 133.5, 133.4, 130.4, 130.4, 129.6, 129.6, 129.3, 129.2, 128.3, 127.5, 126.4, 126.3, 125.1, 121.9, 104.1, 104.0, 44.2, 44.2, 38.8, 38.7, 38.6, 38.5, 26.8, 26.7, 25.0, 24.4, 23.3, 23.2, 14.3, 14.1. HRMS (EI-TOF) calcd for $C_{25}H_{26}N_2O$ (M^+):370.2045, found: 370.2044.

(*E*)-3-Benzyl-5-benzylidene-3-methyl-1-(quinolin-8-yl)pyrrolidin-2-one (3e). 29.91 mg. Yield, 74%. The ratio of two isomers was 2:1 as determined by ^{1}H NMR. Rf_1 = 0.50, Rf_2 = 0.52 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.79–8.80 (m, 2H), 8.09–8.14 (m, 2H), 7.80–7.87 (m, 2H), 7.49–7.61 (m, 3H), 7.31–7.34 (m, 3H), 7.00–7.26 (m, 14H), 6.92–7.11 (m, 6H), 5.22 (s, 1H), 4.97 (s, 1H), 3.15–3.27 (m, 4H), 2.74–3.02 (m, 4H), 1.53 (s, 3H), 1.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.2, 178.6, 150.1, 150.0, 143.2, 143.2, 141.7, 141.7, 136.5, 136.4, 135.9, 135.8, 135.1, 132.2, 132.0, 129.7, 129.3, 129.3, 128.6, 128.4, 128.3, 128.2, 127.5, 127.3, 127.2, 127.1, 126.8, 126.5, 125.7, 125.5, 125.3, 124.2, 124.1, 120.9, 120.8, 103.8, 103.0, 44.9, 44.5, 43.2, 42.1, 36.6, 36.2, 24.5, 23.7. HRMS (EI-TOF) calcd for $C_{28}H_{24}N_2O$ (M^+): 404.1889, found: 404.1893.

(*E*)-5-Benzylidene-3-methyl-3-(4-methylbenzyl)-1-(quinolin-8-yl)pyrrolidin-2-one (3f). 28.44 mg. Yield, 68%. The ratio of two isomers was 2:1 as determined by ^{1}H NMR. Rf_1 = 0.50, Rf_2 = 0.52 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.85–8.88 (m, 2H), 8.17–8.22 (m, 2H), 7.89–7.94 (m, 2H), 7.58–7.70 (m, 3H), 7.34–7.44 (m, 3H), 7.00–7.25 (m, 18H), 5.30 (s, 1H,), 5.07 (s, 1H), 3.20–3.46 (m, 4H), 2.78–3.01 (m, 4H), 2.36 (s, 6H), 1.59 (s, 3H), 1.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.4, 179.8, 151.2, 151.1, 144.3, 144.3, 142.9, 137.0, 136.9, 136.3, 136.1, 136.0, 134.4, 133.3, 133.2, 130.7, 130.4, 130.3, 130.2, 129.6, 129.5, 129.3, 129.2, 129.0, 128.9, 128.3, 128.2, 127.6, 127.5, 126.4, 125.2, 125.1, 121.9, 121.8, 104.8, 104.1, 45.9, 45.5, 43.7, 42.8, 37.7, 37.2, 25.6, 23.9, 21.2. HRMS (EI-TOF) calcd for $C_{29}H_{26}N_2O$ (M^+): 418.2045, found: 418.2044.

(*E*)-5-Benzylidene-3-(4-fluorobenzyl)-3-methyl-1-(quinolin-8-yl)pyrrolidin-2-one (3g). 23.64 mg. Yield, 56%. The ratio of two isomers was 2:1 as determined by ^{1}H NMR. Rf_1 = 0.51, Rf_2 = 0.52 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.82 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.80 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 7.90 (dd, J_1 = 1.6 Hz; J_2 = 8.0 Hz, 1H), 7.85 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.17–7.47 (m, 17H), 6.33–6.56 (m, 7H), 6.09 (d, J = 7.6 Hz, 2H), 5.69 (s, 1H), 5.51 (s, 1H), 2.87–3.30 (m, 8H), 1.57 (s, 3H), 1.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.4, 180.9, 150.0, 150.0, 143.7, 143.5, 138.6, 138.4, 137.7, 137.6, 135.7, 135.7, 134.9, 134.8, 134.3, 134.2, 130.8, 130.5, 129.3, 129.2, 128.8, 128.7, 128.3, 128.3, 128.2, 128.0, 127.9, 126.9, 126.6, 126.1, 125.9, 125.6, 125.5, 125.0, 124.8, 121.2, 121.1, 104.0, 103.2, 45.4, 44.4, 43.0, 40.6, 39.8, 29.8, 25.0, 23.0. HRMS (EI-TOF) calcd for $C_{28}H_{23}FN_2O$ (M^+): 422.1794, found: 422.1796.

(*E*)-5-Benzylidene-3-methyl-3-(naphthalen-2-yl-methyl)-1-(quinolin-8-yl)pyrrolidin-2-one (3h). 33.16 mg. Yield, 73%. The ratio of two isomers was 1.7:1 as determined by ^{1}H NMR. Rf_1 = 0.48, Rf_2 = 0.50 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.81 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.79 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.43 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 7.6 Hz, 1H), 7.88–7.92 (m, 3H), 7.79–7.84 (m, 3H), 7.43–7.60 (m, 8H), 7.37–7.39 (m, 2H), 7.21–7.30 (m, 3H), 7.06 (t, J = 8.0 Hz, 1H), 6.76 (dd, J_1 = 1.2 Hz; J_2 = 7.6 Hz, 1H), 6.43–6.59 (m, 3H), 6.30–6.37 (m, 3H), 5.93 (d, J = 7.6 Hz, 2H) 5.61 (s, 1H), 5.33 (s, 1H), 3.92 (d, J = 14.4 Hz, 1H), 3.73 (d, J = 14.0 Hz, 1H), 3.55 (d, J = 14.0 Hz, 1H), 3.44 (d, J = 14.0 Hz, 1H), 2.90–3.11 (m, 4H), 1.67 (s, 3H), 1.48 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.8, 181.0, 149.9, 149.9, 143.7, 143.3, 138.8, 138.4, 135.7, 135.7, 135.0, 134.7, 134.4, 134.1, 134.0, 134.0, 133.9, 133.6, 133.2, 129.3, 129.3, 129.2, 129.0, 128.8, 128.8, 128.6, 128.2, 128.1, 128.1, 128.0, 127.8, 127.8, 127.6, 127.6, 127.4, 126.1, 126.0, 125.8, 125.6, 125.6, 125.5, 124.9, 124.9, 124.7, 124.6, 121.2, 121.0, 104.0, 103.4, 46.3, 46.1, 40.3, 40.3, 39.5, 37.9, 25.4, 23.6. HRMS (EI-TOF) calcd for $C_{32}H_{26}N_2O$ (M^+): 454.2045, found: 454.2043.

(*E*)-5-Benzylidene-3-methyl-3-phenethyl-1-(quinolin-8-yl)-pyrrolidin-2-one (3i). 29.28 mg. Yield, 70%. The ratio of two isomers was 1:1.2 as determined by ^{1}H NMR. Rf_1 = 0.51, Rf_2 = 0.53 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.88 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.84 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H,), 8.22 (s, 1H), 8.20 (s, 1H), 7.94 (d, J = 2.0 Hz, 1H), 7.92 (d, J = 1.2 Hz, 1H), 7.63–7.73 (m, 4H), 7.38–7.43 (m, 2H), 7.18–7.29 (m, 14H), 7.11 (d, J = 8.0 Hz, 6H), 5.30 (s, 1H, *Z*-isomer), 5.28 (s, 1H, *E*-isomer), 3.03–3.41 (m, 4H), 2.72–2.97 (m, 4H), 2.09–2.20 (m, 4H), 1.59 (s, 3H), 1.49 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.2, 180.2, 151.2, 151.1, 144.3, 143.0, 142.7, 141.9, 137.0, 136.2, 133.5, 133.3, 130.4, 130.4, 129.6, 129.3, 129.3, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.6, 127.6, 126.4, 126.4, 126.0, 125.8, 125.3, 121.9, 104.4, 104.3, 44.4, 44.3, 41.1, 40.8, 39.0, 38.6, 31.1, 31.0, 24.9, 24.5. HRMS (EI-TOF) calcd for $C_{29}H_{26}N_2O$ (M^+): 418.2045, found: 418.2044.

(*E*)-5-Benzylidene-3-(3-(2,5-dimethylphenoxy)p-ropyl)-3-methyl-1-(quinolin-8-yl)pyrrolidin-2-one (3j). 45.24 mg. Yield, 95%. The ratio of two isomers was 1:1.1 as determined by ^{1}H NMR. Rf_1 = 0.50, Rf_2 = 0.52 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.87 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.79 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.16–8.20 (m, 2H), 7.90–7.92 (m, 2H), 7.61–7.70 (m, 4H), 7.36–7.42 (m, 2H), 7.21–7.22 (m, 4H), 7.07–7.11 (m, 6H), 7.00 (d, J = 7.2 Hz, 2H), 6.63–6.67 (m, 4H), 5.29 (s, 1H, *Z*-isomer), 5.28 (s, 1H), 3.98–4.08 (m, 4H), 3.05–3.40 (m, 4H), 2.29 (d, J = 8.0 Hz, 6H), 2.19 (d, J = 4.0 Hz, 6H), 1.91–2.04 (m, 8H), 1.57 (s, 3H), 1.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.5, 180.4, 157.1, 156.9, 151.2, 151.1, 144.3, 144.2, 143.0, 143.0, 137.0, 136.6, 136.5, 136.2, 136.1, 133.4, 133.2, 130.5, 130.4, 130.3, 129.6, 129.6, 129.4, 129.3, 128.4, 128.0, 128.0, 127.6, 127.6, 126.4, 126.4, 126.1, 126.1, 125.3, 123.7, 121.9, 120.9, 120.7, 112.1, 104.4, 104.4, 68.2, 67.9, 44.1, 38.8, 38.6, 35.4, 35.3, 24.9, 24.8, 24.8, 24.5, 21.5, 20.4, 16.0, 16.0, 13.8. HRMS (EI-TOF) calcd for $C_{32}H_{32}N_2O_2$ (M^+): 476.2464, found: 476.2466.

(*E*)-5-Benzylidene-3-methyl-3-phenyl-1-(quino-lin-8-yl)-pyrrolidin-2-one (3k). 24.19 mg. Yield, 62%. The ratio of two isomers was 1.1:1 as determined by ^{1}H NMR. Rf_1 = 0.59, Rf_2 = 0.57 (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.91 (d, J = 1.2 Hz, 1H), 8.90 (d, J = 0.8 Hz, 1H), 8.23 (d, J = 1.6 Hz, 1H), 8.21 (d, J = 1.6 Hz, 1H), 7.96 (dd, J_1 = 1.6 Hz; J_2 = 2.8 Hz, 1H), 7.94 (dd, J_1 = 1.6 Hz; J_2 = 2.8 Hz, 1H), 7.75–7.83 (m, 3H), 7.67–7.71 (m, 3H), 7.58–7.61 (m, 2H), 7.36–7.46 (m, 7H), 7.28 (d, J = 7.6 Hz, 2H), 7.19–7.23 (m,4H), 7.05–7.12 (m, 5H), 5.36 (s, 1H), 5.31 (s, 1H), 3.65–3.74 (m, 2H), 3.67 (dd, J_1 = 2.0 Hz; J_2 = 16.0 Hz, 1H), 3.44 (dd, J_1 = 2.0 Hz; J_2 = 16.4 Hz, 1H), 1.95 (s, 3H), 1.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.1, 178.8, 151.2, 151.1, 144.3, 144.1,

142.5, 142.4, 136.8, 136.8, 136.2, 136.2, 133.4, 133.3, 130.5, 130.4, 129.6, 129.6, 129.4, 129.4, 128.7, 128.5, 128.3, 127.7, 127.6, 127.0, 126.9, 126.8, 126.7, 126.4, 126.1, 126.1, 126.0, 125.3, 122.0, 121.9, 104.7, 104.6, 48.5, 48.4, 43.6, 42.6, 25.9, 25.1. HRMS (EI-TOF) calcd for $C_{27}H_{22}N_2O$ (M^+):390.1732, found: 390.1732.

(*E*)-5-Benzylidene-3-butyl-3-phenyl-1-(quinolin-8-yl)pyrrolidin-2-one (3l). 39.33 mg. Yield, 81%. The ratio of two isomers was 1.2:1 as determined by ^{1}H NMR. $Rf_1 = 0.51$, $Rf_2 = 0.51$ (hexane/EtOAc = 2:1). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 8.90 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.85 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.22 (s, 1H), 8.20 (d, J = 0.8 Hz, 1H), 7.91–7.96 (m, 2H), 7.78–7.80 (m, 2H), 7.69–7.75 (m, 2H), 7.62–7.64 (m, 4H), 7.35–7.45 (m, 6H), 7.21–7.29 (m, 6H), 7.08–7.16 (m, 6H), 5.31 (s, 1H), 5.29 (s, 1H), 3.49–3.72 (m, 4H), 2.16–2.38 (m, 4H), 1.49–1.58 (m, 4H), 1.33–1.42 (m, 4H), 0.92–0.96 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.0, 177.9, 151.1, 151.0, 144.3, 144.0, 142.8, 142.7, 136.9, 136.9, 136.1, 133.4, 133.4, 130.5, 130.4, 129.6, 129.6, 129.3, 129.3, 128.6, 128.5, 128.4, 128.3, 127.7, 127.6, 126.9, 126.8, 126.7, 126.5, 126.4, 126.4, 125.3, 125.3, 121.9, 121.9, 104.2, 104.0, 52.1, 52.0, 40.5, 39.2, 38.9, 26.9, 26.8, 23.2, 23.2, 14.1, 14.1. HRMS (EI-TOF) calcd for $C_{30}H_{28}N_2O$ (M^+):432.2202, found:432.2205.

(*E*)-7-Benzylidene-6-(quinolin-8-yl)-6-azaspiro[3.4]octan-5-one (3m). 19.39 mg. Yield, 57%. R_f 0.52 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.21 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.93 (dd, J_1 = 2.4 Hz; J_2 = 7.2 Hz, 1H), 7.64–7.69 (m, 2H), 7.42 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.22–7.24 (m, 2H), 7.07–7.12 (m, 3H), 6.25 (s, 1H), 3.56 (dd, J_1 = 2.0 Hz; J_2 = 16.4 Hz, 1H), 3.40 (dd, J_1 = 2.0 Hz; J_2 = 16.4 Hz, 1H), 2.82–2.85 (m, 1H), 2.69–2.73 (m, 1H), 2.04–2.24 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.8, 151.2, 144.2, 143.2, 137.0, 133.4, 130.4, 129.6, 129.2, 128.3, 127.6, 126.4, 125.2, 125.4, 121.9, 104.0, 45.6, 40.2, 32.3, 31.8, 16.3. HRMS (EI-TOF) calcd for $C_{23}H_{20}N_2O$ (M^+): 340.1576, found: 340.1574.

(*E*)-3-Benzylidene-2-(quinolin-8-yl)-2-azaspiro[4.4]nonan-1-one (3n). 23.47 mg. Yield, 68%. R_f 0.51 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.21 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.93 (dd, J_1 = 1.6 Hz; J_2 = 8.0 Hz, 1H), 7.64–7.71 (m, 2H), 7.43 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.23 (t, J = 8.0 Hz, 2H), 7.06–7.11 (m, 3H), 5.27 (s, 1H), 3.30 (dd, J_1 = 1.6 Hz; J_2 = 16.0 Hz, 1H), 3.16 (dd, J_1 = 2.4 Hz; J_2 = 16.0 Hz, 1H), 2.33–2.37 (m, 1H), 2.20–2.23 (m, 1H), 1.79–1.94 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 151.2, 144.3, 143.5, 137.1, 136.2, 133.5, 130.4, 129.6, 129.2, 128.3, 127.6, 126.4, 125.2, 121.8, 104.4, 51.2, 41.1, 38.4, 38.0, 25.5, 25.5. HRMS (EI-TOF) calcd for $C_{24}H_{22}N_2O$ (M^+): 354.1732, found: 354.1733.

(*E*)-3-Benzylidene-2-(quinolin-8-yl)-2-azaspiro[4.5]decan-1-one (3o). 29.82 mg. Yield, 81%. R_f 0.54 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.85 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.19 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.91 (dd, J_1 = 2.0 Hz; J_2 = 7.6 Hz, 1H), 7.64–7.68 (m, 2H), 7.40 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.22–7.26 (m, 2H), 7.08–7.14 (m, 3H), 6.25 (s, 1H), 3.29 (dd, J_1 = 1.6 Hz; J_2 = 16.0 Hz, 1H), 3.12 (dd, J_1 = 2.0 Hz; J_2 = 16.0 Hz, 1H), 1.92–1.95 (m, 2H), 1.81–1.89 (m, 4H), 1.69–1.72 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.9, 150.1, 143.3, 142.4, 136.1, 135.1, 132.4, 129.5, 128.6, 128.2, 127.4, 126.6, 125.4, 124.2, 120.9, 103.1, 44.3, 36.1, 32.6, 31.0, 28.8, 24.4, 21.3. HRMS (EI-TOF) calcd for $C_{25}H_{24}N_2O$ (M^+): 368.1889, found: 368.1895.

(*E*)-3,3-Dimethyl-5-(4-methylbenzylidene)-1(quinolin-8-yl)pyrrolidin-2-one (4a). 28.40 mg. Yield, 83%. R_f 0.51 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.21 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.92 (dd, J_1 = 1.6 Hz; J_2 = 8.0 Hz, 1H), 7.63–7.70 (m, 2H), 7.42 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.02 (d, J_1 = 8.0 Hz; J_2 = 20.0 Hz, 4H), 5.25 (s, 1H), 3.24 (dd, J_1 = 1.6 Hz; J_2 = 16.0 Hz, 1H), 3.09 (dd, J_1 = 1.6 Hz; J_2 = 16.0 Hz, 1H), 2.28 (s, 3H), 1.53 (s, 3H), 1.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 151.1, 142.2, 136.2, 134.9, 134.1, 133.4, 130.5, 129.6, 129.2, 129.0, 128.6, 127.5, 126.4, 121.8, 104.3, 41.2, 40.9, 26.1, 25.7, 21.1. HRMS (EI-TOF) calcd for $C_{23}H_{22}N_2O$ (M^+): 342.1732, found: 342.1731.

(*E*)-3,3-Dimethyl-5-(3-methylbenzylidene)-1-(quinolin-8-yl)pyrrolidin-2-one (4b). 25.32 mg. Yield, 74%. R_f 0.0.51 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (dd, J_1 = 1.2 Hz; J_2 = 4.0 Hz, 1H), 8.20 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.93 (dd, J_1 = 1.6 Hz; J_2 = 7.2 Hz, 1H), 7.63–7.69 (m, 2H), 7.42 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.89–6.94 (m, 3H), 5.24 (s, 1H), 3.25 (dd, J_1 = 1.6 Hz; J_2 = 15.6 Hz, 1H), 3.12 (dd, J_1 = 2.0 Hz; J_2 = 16.0 Hz, 1H), 2.27 (s, 3H), 1.53 (s, 3H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 151.2, 144.3, 142.8, 137.8, 136.9, 136.1, 133.4, 130.4, 129.6, 129.2, 128.5, 128.2, 126.4, 126.0, 124.5, 121.8, 104.5, 41.2, 40.9, 26.1, 25.7, 21.5. HRMS (EI-TOF) calcd for $C_{23}H_{22}N_2O$ (M^+): 342.1732, found: 342.1731.

(*E*)-3,3-Dimethyl-5-(2-methylbenzylidene)-1-(quinolin-8-yl)pyrrolidin-2-one (4c). 21.21 mg. Yield, 62%. R_f 0.50 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 7.89 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.43 (dd, J_1 = 1.2 Hz; J_2 = 8.0 Hz, 1H), 7.32 (dd, J_1 = 1.2 Hz; J_2 = 7.2 Hz, 1H), 7.27 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.16 (dd, J_1 = 7.2 Hz; J_2 = 7.6 Hz, 1H), 6.49–6.52 (m, 2H), 6.11–6.18 (m, 2H), 5.56 (s, 1H), 3.08 (dd, J_1 = 1.6 Hz; J_2 = 14.8 Hz, 1H), 2.88 (d, J_1 = 1.6 Hz; J_2 = 14.8 Hz, 1H), 1.95 (s, 3H), 1.52 (s, 3H), 1.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.3, 150.0, 143.9, 138.7, 135.6, 135.3, 134.2, 134.2, 129.2, 129.0, 128.6, 128.0, 128.0, 125.5, 125.4, 123.5, 121.1, 102.7, 43.4, 40.8, 25.1, 25.1, 20.1. HRMS (EI-TOF) calcd for $C_{23}H_{22}N_2O$ (M^+): 342.1732, found: 342.1733.

(*E*)-5-(4-Methoxybenzylidene)-3,3-dimethyl-1-(quinolin-8-yl)pyrrolidin-2-one (4d). 22.56 mg. Yield, 62%. R_f 0.42 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 8.21 (dd, J_1 = 1.6 Hz; J_2 = 8.0 Hz, 1H), 7.92 (dd, J_1 = 2.0 Hz; J_2 = 7.2 Hz, 1H), 7.65–7.67 (m, 2H), 7.42 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.03 (d, J = 9.2 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.23 (s, 1H), 3.76 (s, 3H), 3.22 (dd, J_1 = 1.6 Hz; J_2 = 16.0 Hz, 1H), 3.08 (dd, J_1 = 2.0 Hz; J_2 = 16.0 Hz, 1H), 1.53 (s, 3H), 1.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 157.3, 151.1, 144.3, 141.3, 136.2, 133.4, 130.8, 129.6, 129.2, 128.7, 126.4, 121.8, 113.8, 113.8, 103.9, 55.3, 41.0, 40.9, 26.0, 25.7. HRMS (EI-TOF) calcd for $C_{23}H_{22}N_2O_2$ (M^+): 358.1681, found: 358.1683.

(*E*)-5-(4-Fluorobenzylidene)-3,3-dimethyl-1-(quinolin-8-yl)pyrrolidin-2-one (4e). 24.58 mg. Yield, 71%. R_f 0.50 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (dd, J_1=1.2 Hz; J_2=3.6 Hz, 1H), 8.22 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.94 (dd, J_1=2.8 Hz; J_2=7.2 Hz, 1H), 7.64–7.70 (m, 3H), 7.44 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 7.04–7.09 (m, 2H), 6.90–6.94 (m, 2H), 5.24 (s, 1H), 3.21 (dd, J_1=1.2 Hz; J_2=16.0 Hz, 1H), 3.07 (dd, J_1=1.6 Hz; J_2=16.0 Hz, 1H), 1.53 (s, 3H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.0, 160.5 (d, J_{C-F}=247.1 Hz), 151.1, 142.6, 136.2, 133.3, 133.0 (d, J_{C-F}=5.4 Hz), 131.8 (d, J_{C-F}=7.9 Hz), 130.4, 129.6, 129.3, 128.9 (d, J_{C-F}=7.2 Hz), 126.4, 121.9, 115.1 (d, J_{C-F}=20.9 Hz), 103.2, 41.0, 40.8, 26.1, 25.7. HRMS (EI-TOF) calcd for $C_{22}H_{19}FN_2O$ (M^+): 346.1481, found: 346.1478.

(*E*)-5-(4-Chlorobenzylidene)-3,3-dimethyl-1-(quinolin-8-yl)pyrrolidin-2-one (4f). 22.45 mg. Yield, 62%. R_f 0.48 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.21 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H), 7.93 (dd, J_1=2.4 Hz; J_2=7.2 Hz, 1H), 7.65–7.68 (m, 2H), 7.43 (dd, J_1=4.0 Hz; J_2=8.4 Hz, 1H), 7.19 (d, J=8.4 Hz, 2H), 7.02 (d, J=8.4 Hz, 2H), 5.22 (s, 1H), 3.21 (dd, J_1=1.6 Hz; J_2=16.0 Hz, 1H), 3.07 (dd, J_1=2.0 Hz; J_2=16.0 Hz, 1H), 1.53 (s, 3H), 1.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.0, 151.2, 144.3, 143.5, 136.2, 135.6, 133.2, 130.6, 130.4, 129.6, 129.4, 128.7, 128.4, 126.4, 121.9, 103.2, 41.1, 40.8, 26.1, 25.7. HRMS (EI-TOF) calcd for $C_{22}H_{19}ClN_2O$ (M^+): 362.1186, found: 362.1183.

(*E*)-5-(4-Bromobenzylidene)-3,3-dimethyl-1-(quinolin-8-yl)pyrrolidin-2-one (4g). 21.52 mg. Yield, 53%. R_f 0.44 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.21 (dd, J_1=2.0 Hz; J_2=8.4 Hz,, 1H), 7.93 (dd, J_1=3.2 Hz; J_2=6.8 Hz, 1H), 7.63–7.68 (m, 2H), 7.43 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 7.33 (d, J=8.4 Hz, 2H), 6.96 (d, J=8.8 Hz, 2H), 5.20 (s, 1H), 3.20 (dd, J_1=2.0 Hz; J_2=16.0 Hz, 1H), 3.07 (dd, J_1=2.0 Hz; J_2=16.0 Hz, 1H), 1.53 (s, 3H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 151.2, 144.2, 143.7, 136.2, 136.0, 133.2, 131.3, 130.4, 129.6, 129.4, 129.1, 126.4, 121.9, 118.6, 103.2, 41.1, 40.8, 26.1, 25.7. HRMS (EI-TOF) calcd for $C_{22}H_{19}BrN_2O$ (M^+): 406.0681, found: 406.1677.

(*E*)-3,3-Dimethyl-1-(quinolin-8-yl)-5-(thiophen-2-ylmethylene)pyrrolidin-2-one (4h). 14.03 mg. Yield, 42%. R_f 0.47 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.86 (dd, J_1=1.6 Hz; J_2=4.0 Hz,, 1H), 8.01 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.62 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 7.42 (dd, J_1=1.6 Hz; J_2=7.6 Hz, 1H), 7.30–7.36 (m, 2H), 6.57 (dd, J_1=0.8 Hz; J_2=4.4 Hz, 1H), 6.11 (dd, J_1=3.2 Hz; J_2=5.6 Hz, 1H), 5.62–5.63 (m, 1H), 5.57 (d, J=1.2 Hz, 1H), 3.04 (dd, J_1=1.6 Hz; J_2=15.2 Hz, 1H), 2.87 (dd, J_1=1.6 Hz; J_2=15.2 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.3, 150.3, 144.0, 141.1, 135.7, 134.2, 129.2, 128.8, 128.2, 127.5, 126.2, 125.7, 125.4, 123.5, 121.4, 95.1, 43.5, 40.5, 25.4, 25.1. HRMS (EI-TOF) calcd for $C_{20}H_{18}N_2OS$ (M^+): 334.1140, found: 334.1138.

(*E*)-3,3-Dimethyl-1-(quinolin-8-yl)-5-(thiophen-3-ylmethylene)pyrrolidin-2-one (4i). 14.70 mg. Yield, 44%. R_f 0.47 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.88 (dd, J_1=1.6 Hz; J_2=4.4 Hz,, 1H), 8.21 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.93 (dd, J_1=3.2 Hz; J_2=6.8 Hz, 1H), 7.65–7.67 (m, 2H), 7.42 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 7.21 (dd, J_1=1.2 Hz; J_2=5.2 Hz, 1H), 6.91 (dd, J_1=0.8 Hz; J_2=4.8 Hz, 1H), 6.86 (d, J=2.0 Hz, 1H), 5.31 (s, 1H), 3.21 (dd, J_1=2.0 Hz; J_2=16.0 Hz, 1H), 3.07 (dd, J_1=2.0 Hz; J_2=16.0 Hz, 1H), 1.55 (s, 3H), 1.45 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 151.2, 144.3, 142.4, 137.8, 136.1, 133.3, 130.4, 129.6, 129.3, 127.8, 126.4, 125.0, 121.9, 119.2, 98.8, 41.2, 40.8, 26.3, 25.8. HRMS (EI-TOF) calcd for $C_{20}H_{18}N_2OS$ (M^+): 334.1140, found: 334.1141.

(*E*)-3,3-Dimethyl-5-(2-methylallylidene)-1-(quinolin-8-yl)-pyrrolidin-2-one (4j). 13.14 mg. Yield, 45%. R_f 0.40 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.20 (dd, J_1=1.6 Hz; J_2=4.4 Hz, 1H), 7.91 (dd, J_1=2.0 Hz; J_2=7.2 Hz, 1H), 7.59–7.65 (m, 2H), 7.42 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 4.85 (s, 1H), 4.71 (s, 1H), 4.56 (s, 1H), 3.19 (dd, J_1=1.6 Hz; J_2=16.4 Hz, 1H), 3.04 (dd, J_1=1.6 Hz; J_2=16.4 Hz, 1H), 1.86 (s, 3H), 1.51 (s, 3H), 1.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.3, 151.3, 144.3, 142.2, 140.5, 136.2, 133.3, 130.4, 129.5, 129.2, 126.3, 121.8, 112.7, 106.6, 41.0, 40.6, 26.1, 25.7, 23.4. HRMS (EI-TOF) calcd for $C_{19}H_{20}N_2O$ (M^+): 292.1576, found: 292.1577.

(*E*)-5-(Cyclopropylmethylene)-3,3-dimethyl-1-(quinolin-8-yl)pyrrolidin-2-one (4k). 16.07 mg. Yield, 55%. R_f 0.41 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.82 (dd, J_1=1.6 Hz; J_2=4.0 Hz,, 1H), 8.09 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H), 7.79 (dd, J_1=3.2 Hz; J_2=6.4 Hz, 1H), 7.50–7.54 (m, 2H), 7.33 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 3.62–3.65 (m, 1H), 2.94 (dd, J_1=2.0 Hz; J_2=16.0 Hz, 1H), 2.79 (dd, J_1=2.0 Hz; J_2=15.6 Hz, 1H), 1.44 (s, 3H), 1.34 (s, 3H), 1.18–1.28 (m, 3H), 0.52–0.56 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.9, 151.0, 144.3, 139.4, 136.1, 133.6, 130.2, 129.5, 128.9, 126.3, 121.7, 105.7, 40.6, 38.9, 26.2, 25.8, 9.2, 6.7, 6.6. HRMS (EI-TOF) calcd for $C_{19}H_{20}N_2O$ (M^+): 292.1576, found: 292.1578.

(*E*)-5-(Cyclohexylmethylene)-3,3-dimethyl-1-(quinolin-8-yl)pyrrolidin-2-one (4l). 18.72 mg. Yield, 56%. R_f 0.55 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.86 (dd, J_1=1.6 Hz; J_2=4.0 Hz,, 1H), 8.16 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.86 (dd, J_1=2.8 Hz; J_2=6.4 Hz, 1H), 7.59–7.60 (m, 2H), 7.39 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 4.03–4.02 (m, 1H), 2.89 (dd, J_1=2.0 Hz; J_2=15.6 Hz, 1H), 2.74 (dd, J_1=2.0 Hz; J_2=15.6 Hz, 1H), 2.00–2.08 (m, 1H), 1.53–1.65 (m, 6H), 1.48 (s, 3H), 1.38 (s, 3H), 1.18–1.33 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.1, 150.8, 144.3, 138.5, 136.0, 133.8, 130.2, 129.5, 128.7, 126.2, 121.6, 108.7, 40.6, 38.6, 36.3, 33.8, 33.7, 26.2, 26.1, 26.0, 25.9, 25.6. HRMS (EI-TOF) calcd for $C_{22}H_{26}N_2O$ (M^+): 334.2045, found: 334.2045.

General procedure for the nickel-catalyzed annulation of arylamides/acrylamides 5/8 with terminal alkynes 2 (Table 4, 5 and 6).

A 25 mL sealed tube was charged with *N*-(quinolin-8-yl)-benzamide/*N*-(quinolin-8-yl) acrylamide (0.1 mmol), acetylene (0.3 mmol), $(Cy_3P)_2NiCl_2$ (6.9 mg, 0.01 mmol), Na_2CO_3 (21.2 mg, 0.2 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol), TBAI (110.8 mg, 0.3 mmol) and toluene/1,3,5-trimethylbenzene (1.5 mL). The vial was evacuated and filled with N_2 atmosphere, and stirred at 140 °C/130 °C for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc

(2 mL), filtered through a Celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:5~1:2, v/v), to afford the desired alkylated product.

(*Z*)-3-Benzylidene-5-methyl-2-(quinolin-8-yl)isoindolin-1-one (6a). 29.00 mg. Yield, 80%. R_f 0.18 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.84 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.96 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.87 (d, J=7.6 Hz, 1H), 7.68 (s, 1H), 7.57 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.46 (dd, J_1=1.6 Hz; J_2=7.2 Hz, 1H), 7.37 (d, J=7.6 Hz, 1H), 7.28–7.31 (m, 2H), 6.77 (s, 1H), 6.65–6.67 (m, 1H), 6.50–6.56 (m, 4H), 2.56 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 150.3, 144.4, 143.0, 139.1, 136.2, 135.8, 134.3, 133.7, 130.3, 130.1, 128.9, 128.4, 128.3, 128.2, 126.3, 125.9, 125.7, 123.8, 121.2, 120.0, 106.9, 22.2. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O$ (M^+): 362.1419, found: 362.1420.

(*Z*)-3-Benzylidene-6-methyl-2-(quinolin-8-yl)isoindolin-1-one (6b). 22.09 mg. Yield, 61%. R_f 0.29 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.84 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.96 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H), 7.75–7.79 (m, 2H), 7.57 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.45–7.50 (m, 2H), 7.28–7.31 (m, 2H), 6.74 (s, 1H), 6.64–6.66 (m, 1H), 6.50–6.56 (m, 4H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 150.4, 144.5, 139.4, 136.3, 136.2, 135.8, 134.3, 133.7, 133.3, 130.1, 128.9, 128.5, 128.3, 128.2, 126.3, 125.9, 125.7, 124.0, 121.2, 119.5, 106.7, 21.6. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O$ (M^+): 362.1419, found: 362.1421.

(*Z*)-3-Benzylidene-7-methyl-2-(quinolin-8-yl)isoindolin-1-one (6c). 16.30 mg. Yield, 45%. R_f 0.44 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.97 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H), 7.70 (d, J=6.8 Hz, 1H), 7.51–7.58 (m, 2H), 7.44 (dd, J_1=1.6 Hz; J_2=6.8 Hz, 1H), 7.23–7.33 (m, 3H), 6.76 (s, 1H), 6.64–6.68 (m, 1H), 6.50–6.58 (m, 4H), 2.77 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 150.5, 144.5, 139.4, 138.1, 136.0, 135.8, 134.4, 133.8, 131.8, 131.1, 130.0, 128.8, 128.3, 128.2, 126.3, 125.9, 125.6, 125.6, 121.2, 117.1, 106.5, 17.6. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O$ (M^+): 362.1419, found: 362.1424.

(*Z*)-3-Benzylidene-5-methoxy-2-(quinolin-8-yl)isoindolin-1-one (6d). 28.36 mg. Yield, 75%. R_f 0.10 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.86 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.97 (d, J=8.4 Hz, 1H), 7.89 (d, J=8.4 Hz, 1H), 7.57 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 7.47 (dd, J_1=1.6 Hz; J_2=7.6 Hz, 1H), 7.27–7.33 (m, 3H), 7.10 (dd, J_1=2.0 Hz; J_2=8.4 Hz, 1H), 6.75 (s, 1H), 6.65–6.67 (m, 1H), 6.50–6.57 (m, 4H), 3.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 163.5, 150.2, 144.2, 141.0, 136.1, 136.0, 134.3, 133.6, 130.1, 128.9, 128.2, 128.1, 126.3, 126.0, 125.7, 125.5, 121.3, 121.2, 116.5, 107.0, 103.7, 55.8. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O_2$ (M^+): 378.1368, found: 378.1371.

(*Z*)-3-Benzylidene-6-(dimethylamino)-2-(quinolin-8-yl)-isoindolin-1-one (6e). 22.30 mg. Yield, 57%. R_f 0.24 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.93 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.24 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H), 7.96 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.84 (dd, J_1=1.2 Hz; J_2=7.2 Hz, 1H), 7.69 (dd, J_1=7.6 Hz; J_2=8.0 Hz, 1H), 7.37–7.45 (m, 4H), 7.30–7.33 (m, 2H), 7.23–7.26 (m, 2H), 6.73 (dd, J_1=2.4 Hz; J_2=8.4 Hz, 1H), 5.78 (s, 1H), 3.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.9, 151.5, 151.2, 145.2, 139.3, 136.3, 136.1, 133.3, 132.0, 131.5, 129.6, 129.3, 128.3, 127.0, 126.3, 126.2, 124.1, 123.5, 121.8, 115.6, 108.7, 105.9, 40.6. HRMS (EI-TOF) calcd for $C_{26}H_{21}N_3O$ (M^+): 391.1685, found: 391.1687.

(*Z*)-3-Benzylidene-5,7-dimethyl-2-(quinolin-8-y-l)isoindolin-1-one (6f). 30.47 mg. Yield, 81%. R_f 0.42 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.97 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.56 (d, J=7.6 Hz, 1H), 7.51 (s, 1H), 7.44 (d, J=7.2 Hz, 1H), 7.30 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 7.26 (t, J=4.0 Hz, 1H), 7.12 (s, 1H), 6.73 (s, 1H), 6.64–6.68 (m, 1H), 6.50–6.57 (m, 4H), 2.72 (s, 3H), 2.50 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 150.4, 144.5, 142.4, 139.6, 137.8, 136.1, 135.9, 134.5, 133.9, 132.2, 130.0, 128.8, 128.2, 128.1, 126.3, 125.8, 125.6, 123.3, 121.1, 117.5, 106.1, 22.0, 17.5. HRMS (EI-TOF) calcd for $C_{26}H_{20}N_2O$ (M^+): 376.1576, found: 376.1577.

(*Z*)-3-Benzylidene-5-fluoro-2-(quinolin-8-yl)isoindolin-1-one (6g). 23.86 mg. Yield, 71%. R_f 0.25 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.84 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.97 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 2H), 7.59 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 7.54 (dd, J_1=2.0 Hz; J_2=8.4 Hz, 1H), 7.48 (dd, J_1=1.6 Hz; J_2=7.2 Hz, 1H), 7.23–7.32 (m, 3H), 6.75 (s, 1H), 6.67–6.70 (m, 1H), 6.53–6.56 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.2, 165.8 (d, J_{C-F}=249.6 Hz), 150.4, 144.2, 141.1 (d, J_{C-F}=9.8 Hz), 135.9, 135.3 (d, J_{C-F}=3.5 Hz), 133.9, 133.1, 130.1, 128.9, 128.5, 128.1, 126.4, 126.3 (d, J_{C-F}=4.5 Hz), 126.1, 125.7, 124.4, 121.3, 117.0 (d, J_{C-F}=22.6 Hz), 108.4, 106.9, 106.7. HRMS (EI-TOF) calcd for $C_{24}H_{15}FN_2O$ (M^+): 366.1168, found: 366.1165.

(*Z*)-3-Benzylidene-5-chloro-2-(quinolin-8-yl)isoindolin-1-one (6h). 27.13 mg. Yield, 71%. R_f 0.35 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.84 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.98 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.92 (d, J=8.4 Hz, 1H), 7.86 (d, J=1.6 Hz, 1H), 7.59 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 7.53 (dd, J_1=1.6 Hz; J_2=8.0 Hz, 1H), 7.48 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.28–7.33 (m, 2H), 6.78 (s, 1H), 6.67–6.71 (m, 1H), 6.54 (d, J=4.4 Hz, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.2, 150.3, 144.1, 140.2, 138.7, 136.0, 135.1, 133.8, 133.1, 130.1, 129.5, 128.9, 128.5, 128.1, 126.7, 126.4, 126.3, 125.7, 125.3, 121.3, 120.1, 108.6. HRMS (EI-TOF) calcd for $C_{24}H_{15}ClN_2O$ (M^+): 382.0873, found: 382.0871.

(*Z*)-3-Benzylidene-5-bromo-2-(quinolin-8-yl)isoindolin-1-one (6i). 22.17 mg. Yield, 52%. R_f 0.33 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.83–8.84 (m, 1H), 8.04(s, 1H), 7.98 (d, J=8.0 Hz, 1H), 7.86 (d, J=8.0 Hz, 1H), 7.67–7.73 (m, 1H), 7.60 (d, J=8.4 Hz, 1H), 7.48 (d, J=7.2 Hz, 1H), 7.28–7.33 (m, 2H), 6.78 (s, 1H), 6.67–6.71 (m, 1H), 6.54 (d, J=4.0 Hz, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 150.4, 144.2, 140.3, 135.8, 133.0, 132.3, 130.0, 129.0, 128.9, 128.6, 128.1, 128.1, 127.0, 126.4, 126.3, 125.7, 125.4, 123.1, 121.3, 108.7, 104.3. HRMS (EI-TOF) calcd for $C_{24}H_{15}BrN_2O$ (M^+): 426.0368, found: 426.0366.

(*Z*)-3-Benzylidene-2-(quinolin-8-yl)-5-(trifluoromethyl)-isoindolin-1-one (6j). 25.38 mg. Yield, 61%. R_f 0.36 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.16 (s, 1H), 8.11 (d, J=8.0 Hz, 1H), 7.97 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H), 7.82 (d, J=7.6 Hz, 1H), 7.60 (dd, J_1=1.2 Hz;

J_2=8.0 Hz, 1H), 7.50 (dd, J_1=1.2 Hz; J_2=7.2 Hz, 1H), 7.29–7.33 (m, 2H), 6.90 (s, 1H), 6.68–6.72 (m, 1H), 6.55 (d, J=4.4 Hz, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.8, 150.5, 144.1, 138.9, 135.9, 135.1, 134.2 (d, J_{C-F}=22.4 Hz), 133.7, 132.9, 131.0, 130.0, 128.8 (d, J_{C-F}=14.7 Hz), 128.1, 126.4, 126.4, 125.9 (d, J_{C-F}=3.5 Hz), 125.7, 125.3, 124.6, 121.4, 117.2 (d, J_{C-F}=3.7 Hz), 109.3. HRMS (EI-TOF) calcd for $C_{25}H_{15}F_3N_2O$ (M^+):416.1136, found: 416.1130.

3-Benzylidene-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[e]isoindol-1-one (6k). 34.24 mg. Yield, 86%. The ratio of **(*E*)-6k/(*Z*)-6k** was 1:1.3 as determined by ^{1}H NMR. ***E*-**R_f 0.21, ***Z*-**R_f 0.21 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz, a mixture of two isomer) δ 9.25 (d, J=8.4 Hz, 1H, *E*-isomer), 9.16 (d, J=8.4 Hz, 1H, *Z*-isomer), 8.93 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H, *E*-isomer), 8.87 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H, *Z*-isomer), 8.26 (dd, J_1=1.6 Hz; J_2=8.4 Hz, 1H, *E*-isomer), 8.11 (d, J=8.8 Hz, 1H, *Z*-isomer), 7.81–8.00 (m, 7H, *Z*- and *E*-isomer), 7.51–7.74 (m, 8H, *Z*- and *E*-isomer), 7.42–7.46 (m, 3H, *Z*- and *E*-isomer), 7.29–7.46 (m, 5H, *Z*- and *E*-isomer), 6.94 (s, 1H, *Z*-isomer), 6.54–6.72 (m, 5H, *Z*- and *E*-isomer), 6.17 (s, 1H, *E*-isomer). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 168.0, 151.3, 150.5, 145.3, 144.6, 138.9, 138.5, 136.4, 136.3, 135.9, 135.4, 135.3, 134.4, 134.0, 133.9, 133.6, 133.0, 133.0, 132.2, 131.7, 130.2, 129.7, 129.6, 129.5, 129.3, 128.9, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.0, 126.8, 126.4, 126.2, 125.7, 124.9, 124.6, 124.6, 122.1, 121.9, 121.2, 120.4, 117.1, 113.6, 109.2. HRMS (EI-TOF) calcd for $C_{28}H_{18}N_2O$ (M^+):398.1419, found: 398.1421.

(*Z*)-6-Benzylidene-5-(quinolin-8-yl)-5,6-dihydro-4H-furo[3,2-c]pyrrol-4-one (6l). 15.21 mg. Yield, 45%. R_f 0.29 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.92 (dd, J_1=1.2 Hz; J_2=4.0 Hz, 1H), 8.09 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.73 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 7.56 (d, J=6.0 Hz, 1H), 7.47 (dd, J_1=1.6 Hz; J_2=7.6 Hz, 1H), 7.42 (d, J=8.0 Hz, 1H), 7.38 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 7.00–7.06 (m, 4H), 6.92–6.95 (m, 2H), 6.70 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.2, 159.8, 151.0, 147.1, 144.7, 143.3, 136.9, 136.2, 136.1, 131.0, 128.9, 128.8, 128.7, 128.2, 127.4, 125.8, 121.6, 115.1, 108.0, 97.6. HRMS (EI-TOF) calcd for $C_{22}H_{14}N_2O_2$ (M^+):338.1055, found: 338.1057.

(*Z*)-4-Benzylidene-5-(quinolin-8-yl)-4H-thieno-[2,3-c]pyrrol-6(5H)-one (6m). 19.12 mg. Yield, 54%. R_f 0.06 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.92 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.09 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.76 (d, J=5.2 Hz, 1H), 7.73 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 7.51 (dd, J_1=1.6 Hz; J_2=7.6 Hz, 1H), 7.42 (t, J=8.4 Hz, 1H), 7.38 (dd, J_1=4.0 Hz; J_2=8.0 Hz, 1H), 7.30 (d, J=5.2 Hz, 1H), 7.26 (s, 1H), 7.08–7.10 (m, 2H), 7.00–7.04 (m, 2H), 6.80 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.2, 151.0, 146.1, 145.4, 144.7, 136.8, 136.3, 136.2, 134.0, 130.9, 129.4, 128.9, 128.9, 128.8, 128.0, 127.3, 125.8, 124.6, 121.6, 104.5. HRMS (EI-TOF) calcd for $C_{22}H_{14}N_2OS$(M^+):354.0827, found: 354.0829.

(*Z*)-3-Benzylidene-2-(quinolin-8-yl)isoindolin-1-one (7a). 29.24 mg. Yield, 84%. R_f 0.30 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.85 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.97–8.00 (m, 2H), 7.89 (d, J=7.6 Hz, 1H), 7.67–7.71 (m, 1H), 7.54–7.60 (m, 2H), 7.48 (dd, J_1=1.6 Hz; J_2=7.6 Hz, 1H), 7.28–7.733 (m, 2H), 6.81 (s, 1H), 6.66–6.68 (m, 1H), 6.51–6.57 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 150.4, 144.4, 138.7, 136.1, 135.8, 134.2, 133.6, 132.3, 130.1, 129.1, 128.9, 128.4, 128.3, 128.2, 126.3, 126.0, 125.7, 124.0, 121.2, 119.7, 107.4. HRMS (EI-TOF) calcd for $C_{24}H_{16}N_2O$ (M^+): 348.1263, found: 348.1264.

(*Z*)-3-(4-Methylbenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7b). 32.23 mg. Yield, 89%. R_f 0.29 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (dd, J_1=1.6 Hz; J_2=4.4 Hz, 1H), 7.93–7.98 (m, 2H), 7.84 (d, J=8.0 Hz, 1H), 7.62–7.66 (m, 1H), 7.50–7.58 (m, 2H), 7.44 (dd, J_1=1.2 Hz; J_2=7.2 Hz, 1H), 7.24–7.28 (m, 2H), 6.77 (s, 1H), 6.41 (d, J=7.6 Hz, 2H), 6.30 (d, J=8.0 Hz, 2H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 150.3, 144.5, 138.8, 135.8, 135.7, 135.7, 134.4, 132.2, 130.6, 130.1, 129.0, 128.9, 128.3, 128.1, 128.1, 127.0, 125.7, 123.9, 121.3, 119.7, 107.7, 20.9. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O$ (M^+): 362.1419, found: 362.1422.

(*Z*)-3-(3-Methylbenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7c). 31.14 mg. Yield, 86%. R_f 0.29 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (dd, J_1=1.6 Hz; J_2=4.4 Hz, 1H), 7.97–8.02 (m, 2H), 7.86 (d, J=7.6 Hz, 1H), 7.65–7.69 (m, 1H), 7.53–7.58 (m, 2H), 7.41 (dd, J_1=1.2 Hz; J_2=7.2 Hz, 1H), 7.32 (dd, J_1=4.0 Hz; J_2=8.4 Hz, 1H), 7.23–7.27 (m, 1H), 6.78 (s, 1H), 6.48–6.58 (m, 3H), 6.27 (s, 1H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 150.5, 144.5, 138.8, 136.0, 135.9, 134.4, 133.5, 132.3, 129.8, 129.4, 129.1, 128.9, 128.3, 126.9, 126.4, 125.7, 125.3, 123.9, 121.3, 119.6, 107.6, 20.7. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O$ (M^+): 362.1419, found: 362.1422.

(*Z*)-3-(2-Methylbenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7d). 29.33 mg. Yield, 81%. R_f 0.29 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.81 (dd, J_1=1.6 Hz; J_2=4.4 Hz, 1H), 8.00 (d, J=7.6 Hz, 1H), 7.90–7.94 (m, 2H), 7.67–7.71 (m, 1H), 7.48–7.58 (m, 3H), 7.25–7.29 (m, 2H), 6.70 (s, 1H), 6.55–6.60 (m, 2H), 6.31 (d, J=7.6 Hz, 1H), 6.13–6.17 (m, 1H), 2.10 (s, 3H), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 150.1, 144.5, 138.5, 136.2, 135.8, 135.6, 133.9, 132.6, 132.2, 130.0, 129.1, 129.0, 128.7, 128.5, 128.2, 126.5, 125.6, 124.0, 123.6, 121.2, 119.7, 106.7, 20.3. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O$ (M^+): 362.1419, found: 362.1422.

(*Z*)-3-(4-Methoxybenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7e). 34.79 mg. Yield, 92%. R_f 0.12 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ8.84 (s, 1H), 7.90 (d, J=4.4 Hz, 2H), 7.78 (d, J=4.4 Hz, 1H), 7.40–7.59 (m, 5H), 7.17–7.22 (m, 1H), 6.67 (s, 1H), 6.40 (s, 2H), 5.99 (s, 2H), 3.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 150.5, 144.5, 138.8, 136.0, 135.9, 134.4, 133.5, 132.3, 129.8, 129.4, 129.1, 128.9, 128.3, 126.9, 126.4, 125.7, 125.3, 123.9, 121.3, 119.6, 107.6, 20.7. HRMS (EI-TOF) calcd for $C_{25}H_{18}N_2O_2$ (M^+): 378.1368, found: 378.1370.

(*Z*)-3-(4-Fluorobenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7f). 29.66 mg. Yield, 81%. R_f 0.22 (hexane/EtOAc=2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ8.84 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 7.98–8.02 (m, 2H), 7.86 (d, J=8.0 Hz, 1H), 7.62–7.70 (m, 2H), 7.56 (t, J=7.2 Hz, 1H), 7.49 (dd, J_1=1.2 Hz; J_2=7.2 Hz, 1H), 7.30–7.35 (m, 2H), 6.73 (s, 1H), 6.49–6.53 (m, 2H), 6.19–6.23 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 160.9 (d, J_{C-F}=245.7 Hz), 150.4, 144.3, 138.6, 136.2 (d, J_{C-F}=50.1 Hz), 134.1, 132.3, 131.3. 130.2, 129.7 (d, J_{C-F}=7.9 Hz), 129.5 (d, J_{C-F}=2.4 Hz), 129.2, 128.9, 128.5, 128.3, 125.8, 124.0, 121.4, 119.7, 113.1 (d, J_{C-F}=

11.9 Hz), 106.1. HRMS (EI-TOF) calcd for $C_{24}H_{15}FN_2O$ (M^+): 366.1168, found: 366.1170.

(*Z*)-3-(4-Chlorobenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7g). 28.27 mg. Yield, 74%. R_f 0.24 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.82 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 7.98–8.02 (m, 2H), 7.86 (d, J = 7.6 Hz, 1H), 7.65–7.70 (m, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.30–7.37 (m, 2H), 6.70 (s, 1H), 6.46 (s, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 150.4, 144.3, 138.5, 136.8, 135.9, 134.1, 132.4, 132.0. 131.8, 130.9, 130.2, 129.3, 128.9, 128.5, 128.3, 126.3, 125.8, 124.0, 121.4, 119.7, 105.8. HRMS (EI-TOF) calcd for $C_{24}H_{15}ClN_2O$ (M^+): 382.0873, found: 382.0868.

(*Z*)-3-(4-Bromobenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (7h). 35.36 mg. Yield, 83%. R_f 0.24 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.81 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 7.97–8.02 (m, 2H), 7.85 (d, J = 7.6 Hz, 1H), 7.65–7.70 (m, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.50 (dd, J_1 = 1.2 Hz; J_2 = 7.2 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.30 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 6.67 (s, 1H), 6.60 (dd, J_1 = 1.6 Hz; J_2 = 6.8 Hz, 2H), 6.38 (d, J = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 150.4, 144.3, 138.4, 136.8, 135.9, 134.1, 132.4, 132.4. 130.2, 129.6, 129.3, 129.2, 128.9, 128.5, 128.3, 125.8, 124.0, 121.5, 120.1, 119.7, 105.8. HRMS (EI-TOF) calcd for $C_{24}H_{15}BrN_2O$ (M^+): 426.0368, found: 426.0363.

(*Z*)-2-(Quinolin-8-yl)-3-(thiophen-2-ylmethylene)isoindolin-1-one (7i). 26.91 mg. Yield, 76%. R_f 0.13 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.85 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.09 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.76 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.62–7.69 (m, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 7.34 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 6.74–6.76 (m, 2H), 6.26 (dd, J_1 = 3.6 Hz; J_2 = 5.2 Hz, 1H), 5.96–5.97 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 150.7, 145.0, 138.7, 135.9, 135.7, 134.2, 132.3, 130.2. 129.6, 129.1, 129.0, 128.8, 128.3, 128.0, 127.4, 125.9, 125.8, 124.1, 121.5, 119.6, 99.8. HRMS (EI-TOF) calcd for $C_{22}H_{14}N_2OS$(M^+):354.0827, found: 354.0828.

(*Z*)-2-(Quinolin-8-yl)-3-(thiophen-3-ylmethylene)isoindolin-1-one (7j). 30.45 mg. Yield, 86%. R_f 0.14 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.84 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.05 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.87 (d, J = 7.2 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.64–7.71 (m, 2H), 7.52–7.56 (m, 2H), 7.39 (t, J = 7.6 Hz, 1H), 7.33 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 6.67 (s, 1H), 6.55 (dd, J_1 = 2.8 Hz; J_2 = 4.8 Hz, 1H), 6.20 (dd, J_1 = 1.2 Hz; J_2 = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 150.5, 144.6, 138.7, 136.2, 136.0, 134.2, 133.9, 132.3. 129.8, 129.1, 129.0, 128.6, 128.2, 127.9, 125.8, 124.0, 123.1, 122.9, 121.4, 119.6, 101.9. HRMS (EI-TOF) calcd for $C_{22}H_{14}N_2OS$(M^+):354.0827, found: 354.0828.

(*Z*)-3-(2-Methylallylidene)-2-(quinolin-8-yl)isoindolin-1-one (7k). 20.29 mg. Yield, 65%. R_f 0.22 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.91 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 8.35 (d, J = 6.8 Hz, 1H), 8.25 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.96–7.99 (m, 2H), 7.76 (dd, J_1 = 1.6 Hz; J_2 = 7.6 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.51–7.56 (m, 2H), 7.45 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 5.34 (s, 1H), 5.30 (s, 1H), 5.21 (s, 1H), 1.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 151.2, 150.5, 139.6, 137.5, 136.3, 136.0, 131.8, 131.4. 130.5, 129.6, 129.4, 129.2, 126.3, 123.9, 123.7, 121.8, 116.5, 114.3, 109.8, 23.3. HRMS (EI-TOF) calcd for $C_{21}H_{16}N_2O$ (M^+): 312.1263, found: 312.1266.

(*Z*)-3-(Cyclopropylmethylene)-2-(quinolin-8-yl)isoindolin-1-one (7l). 14.36 mg. Yield, 46%. R_f 0.15 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.92 (t, J = 2.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.85–7.94 (m, 3H), 7.64–7.66 (m, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.40–7.48 (m, 2H), 5.10 (d, J = 7.6 Hz, 1H), 0.31–0.36 (m, 2H), 0.27–0.30 (m, 1H), 0.07–0.14 (m, 1H), (−0.05)-(−0.01) (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 151.2, 145.5, 138.1, 136.1, 135.4, 135.2, 131.8, 130.6. 129.2, 129.1, 128.1, 127.8, 126.2, 123.7, 121.8, 118.9, 113.8, 8.70, 8.60. HRMS (EI-TOF) calcd for $C_{21}H_{16}N_2O$ (M^+): 312.1263, found: 312.1266.

(*Z*)-3-(Cyclohexylmethylene)-2-(quinolin-8-yl)isoindolin-1-one (7m). 29.04 mg. Yield, 82%. R_f 0.24 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 8.23 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.93–7.99 (m, 2H), 7.80 (dd, J_1 = 1.6 Hz; J_2 = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.58–7.68 (m, 2H), 7.48 (d, J = 7.2 Hz, 1H), 7.42 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 6.46 (d, J = 10.8 Hz, 1H), 1.09–1.47 (m, 5H), 0.84–0.94 (m, 2H), 0.70–0.79 (m, 2H), 0.48–0.53 (m, 1H), 0.04–0.08 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4, 151.2, 145.6, 138.7, 136.1, 135.6, 133.9, 131.9, 130.6. 129.2, 129.2, 128.3, 128.3, 126.3, 123.7, 121.8, 119.3, 115.1, 35.2, 33.2, 33.1, 25.6, 25.5, 25.4. HRMS (EI-TOF) calcd for $C_{24}H_{22}N_2O$ (M^+): 354.1732, found: 354.1733.

(*Z*)-3-Heptylidene-2-(quinolin-8-yl)isoindolin-1-one (7n). 25.29 mg. Yield, 71%. R_f 0.24 (hexane/EtOAc = 2:1). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.90 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.23 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.93–7.96 (m, 2H), 7.80 (dd, J_1 = 1.6 Hz; J_2 = 7.6 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.59–7.63 (m, 1H), 7.48 (t, J = 7.2 Hz, 1H), 7.42 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 6.63 (t, J = 8.0 Hz, 1H), 1.38–1.41 (m, 1H), 1.21–1.27 (m, 2H), 1.03–1.08 (m, 3H), 0.78–0.93 (m, 4H), 0.75 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4, 151.2, 145.6, 138.5, 136.2, 135.4, 135.4, 131.9, 130.7. 129.2, 129.2, 128.3, 128.2, 126.2, 123.7, 121.8, 119.3, 109.7, 31.2, 29.6, 28.7, 25.7, 22.4, 14.0. HRMS (EI-TOF) calcd for $C_{24}H_{24}N_2O$ (M^+): 356.1889, found: 356.1891.

(*Z*)-3-Benzylidene-2-(quinolin-8-yl)-2,3,4,5,6,7-hexahydro-1*H*-isoindol-1-one (9a). 20.07 mg. Yield, 57%. R_f 0.08 (hexane/EtOAc = 2:1). Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.89 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 7.97 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.54 (dd, J_1 = 1.2 Hz; J_2 = 8.0 Hz, 1H), 7.35 (dd, J_1 = 1.2 Hz; J_2 = 7.6 Hz, 1H), 7.30 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.22–7.24 (m, 1H), 6.66 (t, J = 7.2 Hz, 1H), 6.48–6.55 (m, 4H), 6.23 (s, 1H), 2.60–2.64 (m, 2H), 2.46–2.47 (m, 2H), 1.83–1.94 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 149.2, 145.3, 138.9, 134.9, 133.5, 132.7, 129.1, 128.7. 128.6, 127.8, 127.1, 126.7, 125.3, 125.0, 124.7, 120.0, 108.3, 21.2, 21.0, 20.5, 19.5. HRMS (EI-TOF) calcd for $C_{24}H_{20}N_2O$ (M^+): 352.1576, found: 352.1577.

(*Z*)-5-Benzylidene-3-methyl-1-(quinolin-8-yl)-1*H*-pyrrol-2(5*H*)-one (9b). 20.29 mg. Yield, 65%. R_f 0.14 (hexane/EtOAc = 2:1). Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.99 (s, 1H), 8.32 (s, 1H), 7.98 (d, J = 7.2 Hz, 1H), 7.78 (d, J = 6.8 Hz, 1H), 7.72 (d, J_2 = 6.8 Hz, 1H), 7.50 (s, 1H), 7.40 (s, 1H), 7.22–7.33 (m, 5H), 5.88 (s, 1H), 2.17 (s, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 150.8, 144.3, 141.2, 139.6, 135.4, 135.3, 132.3, 131.7. 129.7, 129.4, 129.3, 128.6, 127.4, 126.7, 123.0, 121.9, 113.3, 11.6. HRMS (EI-TOF) calcd for $C_{21}H_{16}N_2O$ (M^+):312.1263, found: 312.1262.

(*Z*)-5-Benzylidene-3-phenyl-1-(quinolin-8-yl)-1*H*-pyrrol-2(5*H*)-one (9c). 23.20 mg. Yield, 62%. R_f 0.50 (hexane/EtOAc=2:1). Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.94 (dd, J_1=1.6 Hz; J_2=4.0 Hz, 1H), 8.26 (dd, J_1=1.2 Hz; J_2=8.0 Hz, 1H), 8.08–8.10 (m, 2H), 7.98 (dd, J_1=1.2 Hz; J_2=8.4 Hz, 1H), 7.85 (s, 1H), 7.83 (dd, J_1=1.2 Hz; J_2=7.2 Hz, 1H), 7.71 (d, J=8.0 Hz, 1H), 7.41–7.47 (m, 5H), 7.34–7.36 (m, 4H), 6.02 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 151.3, 145.2, 140.9, 136.3, 135.5, 134.8, 132.6, 131.6. 131.4, 129.9, 129.6, 129.4, 128.9, 128.7, 128.6, 127.6, 127.4, 127.0, 126.4, 121.9, 115.3. HRMS (EI-TOF) calcd for $C_{26}H_{18}N_2O$ (M^+):374.1416, found: 374.1415.

Procedure of Radical Trapping Experiment (Scheme 1, eq 1).

A 25 mL sealed tube was charged with *N*-(quinolin-8-yl)pivalamide **1a** (0.1 mmol), phenylacetylene **2a** (0.3 mmol), $(Cy_3P)_2NiCl_2$ (6.9 mg, 0.01 mmol), Na_2CO_3 (21.2 mg, 0.2 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol), TBAI (110.8 mg, 0.3 mmol) TEMPO (132.2 mg, 0.8 mmol) or BHT (35.2 mg, 0.8 mmol) and toluene (1.5 mL). The vial was evacuated and filled with N_2 atmosphere, and stirred at 150 °C for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc (2 mL), filtered through a Celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:5~1:2, v/v), to afford the desired alkylated product **3a** (yield=91% and 89%).

Procedure of Control Experiment (Scheme 1, eq 2).

A 25 mL sealed tube was charged with N-(quinolin-8-yl)pivalamide **1a** (0.1 mmol), phenylacetylene **2a** (0.3 mmol), $(Cy_3P)_2NiCl_2$ (6.9 mg, 0.01 mmol), Na_2CO_3 (21.2 mg, 0.2 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol), TBAI (110.8 mg, 0.3 mmol) and toluene (1.5 mL). The vial was evacuated and filled with N_2 atmosphere, and stirred at 150 °C for 5 h. The mixture was then cooled to room temperature, diluted with EtOAc (2 mL). The product **10** was detected by GC-MS (see Supporting Information).

Procedure of Control Experiment (Scheme 1, eq 3).

A 25 mL sealed tube was charged with **10** (0.1 mmol), $(Cy_3P)_2NiCl_2$ (6.9 mg, 0.01 mmol), Na_2CO_3 (21.2 mg, 0.2 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol), TBAI (110.8 mg, 0.3 mmol) and toluene (1.5 mL). The vial was evacuated and filled with N_2 atmosphere, and stirred at 150 °C for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc (2 mL), filtered through a Celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:5~1:2, v/v), to afford the desired alkylated product **3a** (yield=88%).

Procedure of Control Experiment (Scheme 1, eq 4).

A 25 mL sealed tube was charged with **10** (0.1 mmol), Ag_2CO_3 (25.75 mg, 0.01 mmol), TBAI (110.8 mg, 0.3 mmol) or without TBAI and toluene (1.5 mL). The vial was evacuated and filled with N_2 atmosphere, and stirred at 150 °C for 10 min. The mixture was then cooled to room temperature, diluted with EtOAc (2 mL), filtered through a Celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/hexane (1:5~1:2, v/v), to afford the desired alkylated product **3a** (yield=85% and trace).

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