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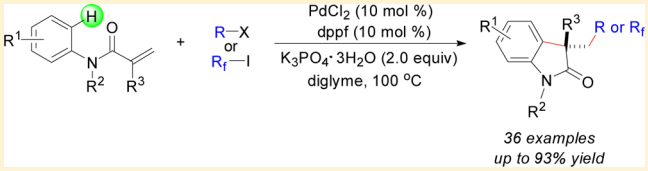
Palladium-Catalyzed Alkylarylation of Acrylamides with Unactivated Alkyl Halides

Hua Wang, Li−Na Guo, and Xin-Hua Duan*

Department of Chemistry, School of Science and MOE Key Laboratory for Nonequilibrium Synthesis and Modulation of Condensed Matter, Xi'an Jiaotong University, Xi'an 710049, China

Supporting Information

ABSTRACT: An efficient palladium-catalyzed alkylarylation of acrylamides with unactivated alkyl halides has been developed. This method is highlighted by its broad substrate scope and excellent functional group tolerance. In addition to alkyl halides, fluoroalkyl halides and benzyl bromides also participated well in this transformation. A detailed mechanistic investigation suggests that a radical pathway is probably involved in the cyclization process.

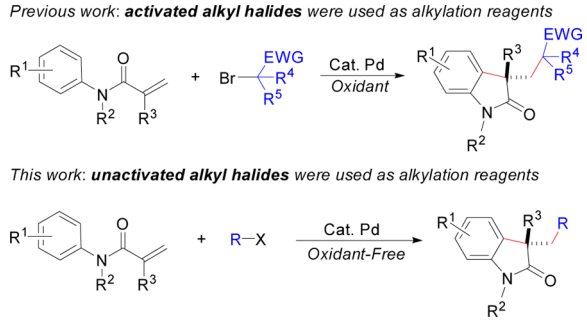


INTRODUCTION

Palladium-catalyzed Heck reactions are one of the most powerful tools for C−C bond formation and have been used widely in organic synthesis.[1] In this field, aryl and vinyl electrophiles are the most commonly used substrates for this transformation. In contrast, alkyl halides, especially unactivated substrates bearing β-hydrogen, are rarely used owing to their facile β-hydride elimination. Recently, some great progress has been made in the more challenging alkyl-Heck reaction.[2−4] For instance, Fu and co-workers developed the first palladium-catalyzed intramolecular alkyl-Heck reaction of primary alkyl electrophiles and monosubstituted alkenes.[2] The palladium-catalyzed radical reactions using alkyl halides as reactants have been previously reported.[5] In 2014, the groups of Alexanian and Zhou independently described the palladium-catalyzed intermolecular Heck-type coupling of unactivated alkyl halides with alkenes, in which a radical rather than a metal-mediated process was involved.[3] Moreover, several radical Heck-type reactions of alkyl halides with alkenes catalyzed by other transition metals have also been reported.[4] Although significant achievements have been made in the alkyl-Heck-type reaction, the palladium-catalyzed tandem coupling/cyclization of unactivated alkyl halides with alkenes is less explored and remains a challenging topic.

Recently, catalytic difunctionalization of alkenes has emerged as an attractive strategy for accessing structurally diverse heterocyclic compounds.[6] Among them, the tandem radical cyclization of acrylamides has attracted much attention and a variety of functionalized oxindoles have been easily synthesized through the difunctionalization of acrylamides with diverse radicals.[7] Furthermore, this tandem radical cyclization strategy has also been applied successfully for the construction of other heterocycles such as dihydroquinolin-2(1*H*)-ones, dihydrofurans, benzoxazines, and so on.[8] More recently, Li and co-workers reported an efficient palladium-catalyzed oxidative difunctionalization of acrylamides with α-carbonyl alkyl bromides for the synthesis of oxindoles (Scheme 1).[9] However,

Scheme 1. Palladium-Catalyzed Cyclization of Acrylamides with Alkyl Halides



the drawbacks of this protocol are the use of a stoichiometric oxidant and limited substrate scopes (only activated alkyl halides were investigated). As part of our ongoing work on tandem cyclization reaction,[8f,g,10] we surmised that the unactivated alkyl halides containing a β-hydrogen might be suitable alkylation reagents in the palladium-catalyzed difunctionalization of activated alkenes. Herein, we wish to report an efficient palladium-catalyzed alkylarylation of acrylamides with various unactivated alkyl halides, giving a series of oxindoles in good to high yields.

RESULTS AND DISCUSSION

To optimize the reaction conditions, *N*-phenyl acrylamide **1a** and iodocyclohexane **2a** were chosen as the initial model substrates. We were pleased to find that the desired product **3a** was isolated in 10% yield when a combination of $PdCl_2$/dppf was used as a catalyst and $K_3PO_4 \cdot 3H_2O$ as a base in toluene at 100 °C (Table 1, entry 1). Further screening of solvents revealed that diglyme is the best choice, affording the desired

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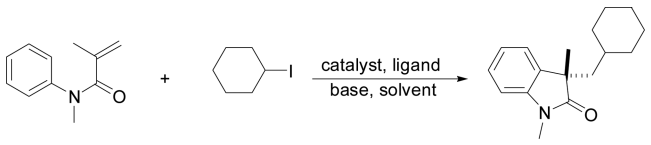
Table 1. Optimization of the Reaction Conditions[a]



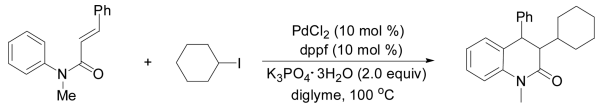
1a 2a 3a

entry	catalyst (mol %)	ligand (mol %)	solvent	yield (%)[b]
1	$PdCl_2$ (10)	dppf (10)	Tol	10
2	$PdCl_2$ (10)	dppf (10)	$PhCF_3$	12
3	$PdCl_2$ (10)	dppf (10)	EtOAc	16
4	$PdCl_2$ (10)	dppf (10)	Et_2O	51
5	$PdCl_2$ (10)	dppf (10)	DME	41
6	$PdCl_2$ (10)	dppf (10)	diglyme	88
7	$PdCl_2$ (10)	dppf (10)	diglyme	76[c]
8	$PdCl_2$ (10)	dppf (10)	diglyme	63[d]
9	$PdCl_2$ (10)	dppf (10)	diglyme	40[e]
10	$PdCl_2$ (10)	dppf (10)	diglyme	55[f]
11	$PdCl_2$(10)	–	diglyme	n.r.
12	$PdCl_2$ (10)	dppe (10)	diglyme	41
13	$PdCl_2$ (10)	PCy_3 (10)	diglyme	21
14	$PdCl_2$ (10)	Ph_3P (10)	diglyme	15
15	$Pd(OAc)_2$ (10)	dppf (10)	diglyme	45
16	$Pd_2(dba)_3$ (10)	dppf (10)	diglyme	55
17	$Pd(PPh_3)_4$ (10)	dppf (10)	diglyme	66
18	$PdCl_2$ (5)	dppf (10)	diglyme	62
19	$PdCl_2$ (10)	dppf (5)	diglyme	40
20	$PdCl_2$ (10)	dppf (10)	diglyme	93[g]
21	$CoCl_2$ (10)	dppf (10)	diglyme	48[g]
22	$FeCl_2$ (10)	dppf (10)	diglyme	40[g]
23	$NiCl_2{\cdot}6H_2O$ (10)	dppf (10)	diglyme	trace[g]

[a]Reaction conditions: catalyst (10 mol %), **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), ligand (10 mol %), $K_3PO_4{\cdot}3H_2O$ (0.4 mmol, 2.0 equiv), solvent (2.0 mL), 100 °C, 24 h, under nitrogen. [b]Yield of isolated product. [c]K_2CO_3 (0.4 mmol, 2.0 equiv) was used. [d]Cs_2CO_3 (0.4 mmol, 2.0 equiv) was used. [e]$NaHCO_3$ (0.4 mmol, 2.0 equiv) was used. [f]Et_3N (0.4 mmol, 2.0 equiv) was used. [g]**2a** (0.5 mmol, 2.5 equiv).

product in 88% yield (entries 2–6). Other inorganic and organic bases were also tested and no better results were obtained (entries 7–10). Notably, the addition of ligand is crucial for the success of this transformation (entry 11). Compared to dppf, other biphosphine ligands such as dppe and monophosphine ligands such as PCy_3 and Ph_3P were less efficient (entries 12–14). Among the palladium(0) and palladium(II) catalysts examined, the simplest $PdCl_2$ showed the best catalytic activity (entries 15–17). Furthermore, the amounts of catalyst and ligand were also adjusted. However, reducing the amount of the palladium catalyst or ligand both resulted in lower yields (entries 18 and 19). Satisfactorily, a slight increase in the ratio of **1a** and **2a** from 1.0/2.0 to 1.0/2.5 resulted in a better yield (entry 20), while a further increase gave a similar result. We confirmed that more than 1.0 equiv of **2a** was required for a good yield due to the formation of the major byproduct bicyclohexyl and other unidentified byproducts. Finally, other inexpensive catalysts such as $CoCl_2$ and $FeCl_2$ were also investigated. However, lower yields of **3a** were obtained (entries 21 and 22). When $NiCl_2{\cdot}6H_2O$ was used, only a trace amount of the desired product was detected.

With the optimal conditions in hand, we then evaluated the scope of acrylamides with **2a** (Table 2). To our delight, a variety of substituted *N*-arylacrylamides proceeded efficiently to afford the cyclized products **3b–t** in moderate to good yields. Both electron-donating and -withdrawing substituents at the *para* position of the aniline moiety were compatible with this transformation (**3b–g**). Remarkably, substrates with highly electron-deficient substituents such as CF_3, CN, and CO_2Et groups on the aniline moiety worked well to furnish the desired products in 80–91% yields (**3d–f**), which cannot be obtained by Liu's protocol.[7d] As expected, the iodo-substituted acrylamides **1h** could not survive the reaction conditions and the corresponding deiodinated oxindole **3a** was obtained in 60% yield. It turned out that the substrate **1h** easily underwent the deiodination process to give **1a** under the present conditions. Fortunately, the chloro-substituted acrylamide gave the desired product **3g** in 76% yield. On the other hand, the steric effect of *ortho*-substituents had no significant effect on this reaction, resulting in good yields (**3i–l**). Polysubstituted acrylamides **1m–o** also reacted smoothly to give the corresponding oxindoles in satisfactory yields, respectively. In addition to the methyl group, substrates bearing other *N*-protecting groups such as benzyl and phenyl also provided the corresponding products in 83% and 80% yields, respectively (**3p** and **3q**). Furthermore, substrates with a benzyl, phenyl, or hydroxymethyl group at the α-position of the acrylamide moiety also led to the corresponding products **3r–3t** in good yields. However, unsubstituted acrylamide **1u** furnished a mixture of unidentified products. It should be mentioned that cinnamamide was also a suitable substrate in this cyclization reaction; the desired dihydroquinolinone was isolated in 39% yield (eq 1).[11]



5a 2a **6a**, 39% (1)

Subsequently, we examined the scope of alkyl halides with **1a** under the palladium-catalyzed system (Table 3). Both cyclic and acyclic iodides reacted smoothly to provide the desired products in moderate to good yields (**4a–f**). As shown in Table 3, the secondary alkyl iodides were more efficient than the primary ones. These results may be attributed to the stability of alkyl radicals (secondary > primary) generated from the corresponding alkyl iodides. With the aim of obtaining more interesting molecules, we applied this cyclization protocol to the perfluoroalkyl iodides.[12] To our delight, the primary perfluoroalkyl iodides were good reaction partners and gave the fluorinated products **4d–f** in good yields, which cannot be easily prepared by previous approaches. Furthermore, the reactions of **1a** with relatively available and unexpensive alkyl bromides were also investigated. It should be mentioned that the addition of NaI was essential for the success of cyclization when secondary alkyl bromides were used.[3h] In the presence of a stoichiometric amount of NaI, the secondary alkyl bromides were also suitable substrates and furnished the desired products in good yields (**4a**, **4g**, and **4h**). We speculated that a more reactive alkyl iodide generated through a Br/I exchange process might be involved in this transformation.[3h,13]

Satisfactorily, the hindered tertiary bromides such as *tert*-butyl bromide and 1-bromoadamantane also worked without NaI to give the desired products but in relatively low yields (**4i** and **4j**). Unfortunately, when alkyl chlorides were used as substrates, no reaction occurred. Remarkably, benzyl bromides also exhibited good reactivities under the present conditions

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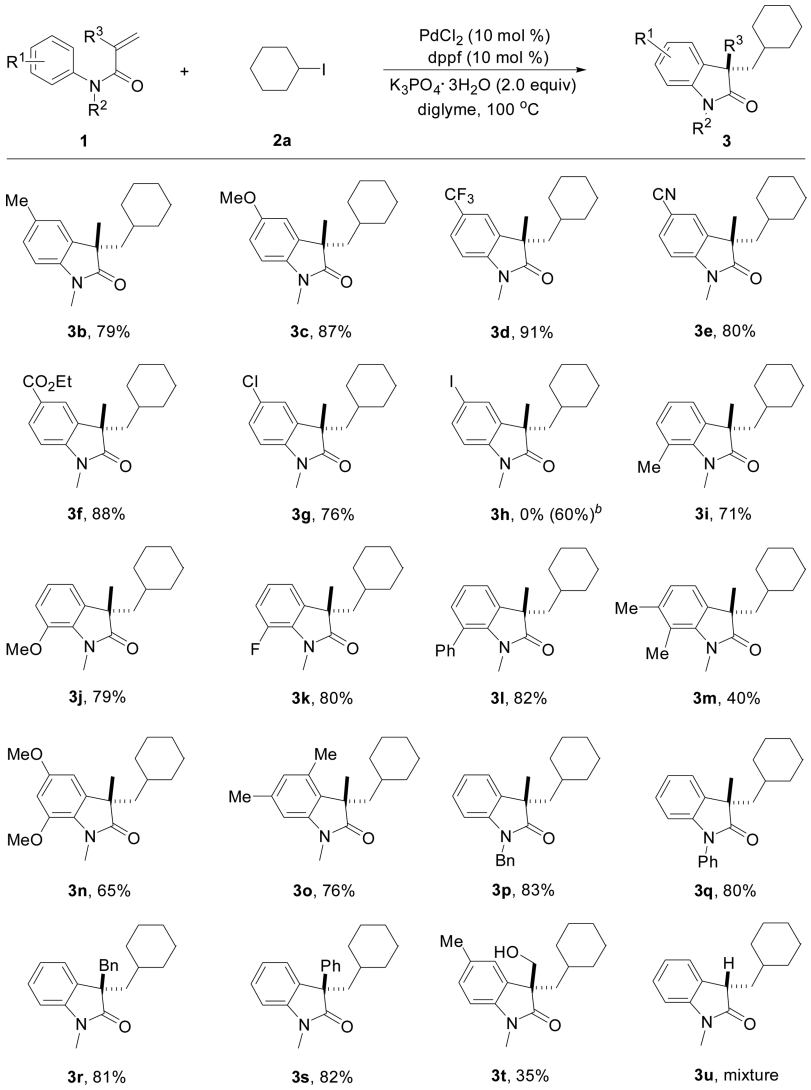
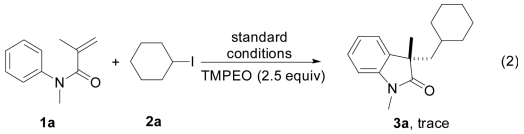
Table 2. Scope of *N*-Arylacrylamides[a]

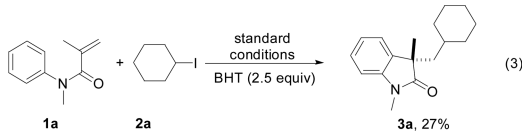


[a]Reaction conditions: 10 mol % of $PdCl_2$, **1** (0.2 mmol, 1.0 equiv), **2a** (0.5 mmol, 2.5 equiv), dppf (10 mol %), $K_3PO_4{\cdot}3H_2O$ (0.4 mmol, 2.0 equiv), diglyme (2.0 mL), 100 °C, 24 h, under nitrogen, yield of isolated product. [b]In this case, the corresponding deiodinated oxindole **3a** was obtained as the major product and the corresponding yield was given in parentheses.

affording the desired products in good yields (**4k–o**). Both electron-donating and -withdrawing groups such as Me, Cl, CN, and CO_2Me on the aromatic moiety of benzyl bromides were tolerated well in this procedure. However, incorporation of a substitute such as ethyl at the benzyl position prevented the formation of oxindole.

To shed some light on the mechanism of this reaction, some control experiments were carried out (for details see the Supporting Information). When a stoichiometric amount of TEMPO or BHT, well-known radical scavengers, was added into the reaction of **1a** and **2a** under the standard conditions, the reaction was suppressed markedly (eqs 2 and 3). Furthermore, the intra- and intermolecular kinetic isotope effect (KIE) experiments were also performed. A negligible KIE (k_H/k_D = 1.0) for





the intra- and intermolecular competition experiments were observed, respectively (eqs 4 and 5). These results indicate that C–H bond cleavage is not the rate-determining step in this reaction. Finally, cyclopropylmethyl bromide and 6-bromo-1-hexene were also treated with **1a** under the standard conditions, respectively. However, only small amounts (<5 isolated yields) of the corresponding pentenyl and cyclopentylethyl substituted oxindoles were obtained due to the low conversion of **1a**.[11] All of these results imply that free-radical substitution was probably involved in this reaction.[3−5] However, an alternative mechanism involving a traditional Pd(0)/Pd(II) catalytic cycle cannot be excluded completely at present.[9a] It should be noted that the recyclability of the palladium catalyst for this reaction was also investigated. After filtering the reaction mixture followed by

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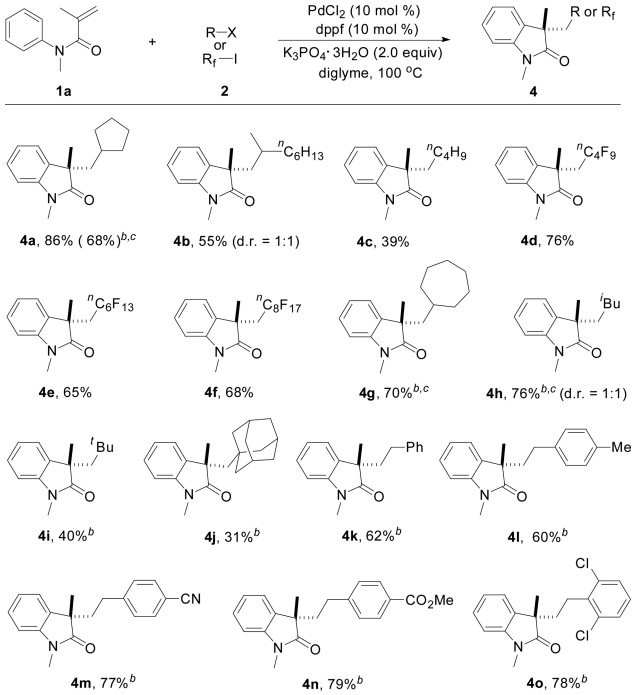
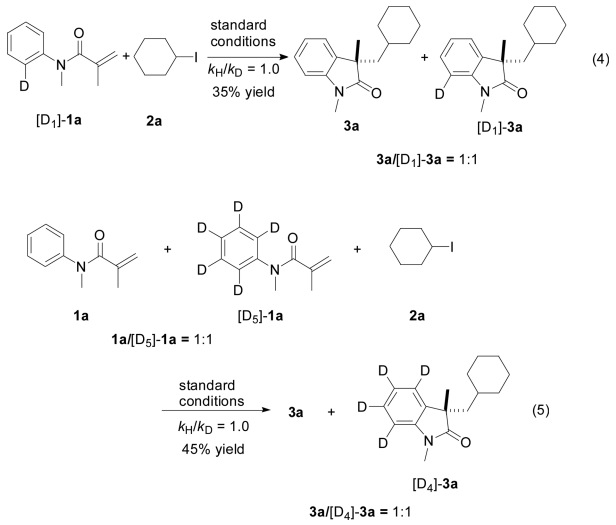
Table 3. Scope of Alkyl, Fluoroalkyl, and Benzyl Halides[a]



[a]Reaction conditions: 10 mol % of $PdCl_2$, **1a** (0.2 mmol, 1.0 equiv), alkyl or fluoroalkyl iodides **2** (0.5 mmol, 2.5 equiv), dppf (10 mol %), $K_3PO_4·3H_2O$ (0.4 mmol, 2.0 equiv), diglyme (2.0 mL), 100 °C, 24 h, under nitrogen, yield of isolated product. [b]The alkyl bromides were used as substrates (for **4a**, the corresponding yield was given in parentheses). [c]3.0 equiv of NaI was used as an additive.



washing to remove organic compounds, the catalyst was reused in the next reaction. In this case, the desired product **3a** was still isolated in 52% yield which suggested that Pd nanoparticles from catalyst death might be the actual active catalyst.[14]

CONCLUSION

In summary, we have demonstrated an efficient Pd-catalyzed alkylarylation of acrylamides with alkyl halides, thus providing an alternative approach to a variety of functionalized oxindoles in moderate to good yields. This protocol shows broad substrate scope and excellent functional group compatibility. Remarkably, not only alkyl iodides and bromides but also perfluoroalkyl iodides and benzyl bromides were compatible with the palladium-catalyzed system. Furthermore, this procedure can be utilized to synthesize some oxindoles, which cannot be accessed by reported methods. Mechanistic investigation revealed that this cyclization reaction proceeds via a cascade radical pathway.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out in sealed tubes filled with nitrogen. Column chromatography was carried out on silica gel. ^1H and ^{13}C NMR spectra were recorded on a 400 M spectrometer in solvents as indicated. The chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard ($CDCl_3$: ^1H NMR: δ = 7.26; ^{13}C NMR: δ = 77.0). IR spectra were recorded on a spectrometer, and only major peaks are reported in cm^{-1}. HRMS data were obtained on a Q-TOF micro spectrometer. All acrylamides **1** were prepared according to a previously reported procedure, and the NMR spectroscopies were in full accordance with the data in the literature.[15] Alkyl iodides were purchased from commercial sources, which were stabilized with copper. 2-Iodo-octane was prepared according to literature.[3a] Alkyl bromides and benzyl bromides were purchased from commercial sources. All of the commercially available compounds were used without further purification.

General Procedure for the Cyclization of Acrylamides with Alkyl Iodides or Fluoroalkyl Iodides. Acrylamides **1** (0.2 mmol, 1.0 equiv), $PdCl_2$ (3.4 mg, 10 mol %), dppf (11.8 mg, 10 mol %), and $K_3PO_4·3H_2O$ (106 mg, 0.4 mmol, 2.0 equiv) were added into an oven-dried sealed tube. The tube was evacuated and backfilled with nitrogen (three times). Then, a solution of alkyl iodides or fluoroalkyl iodides **2** (0.5 mmol, 2.5 equiv) in diglyme (2.0 mL) was injected into the tube by syringe. The tube was then sealed with a Teflon lined cap, and the mixture was stirred at 100 °C for 24 h. The resulting mixture was diluted with EtOAc, and the organic phase was washed successively with H_2O (three times) and brine (one time), then dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc/petroleum ether: 1/20 to 1/10) to give the corresponding product **3** or **4** in yields listed in Tables 2 and 3.

*3-Cyclohexylmethyl-1,3-dimethylindolin-2-one (**3a**).*[7d] Colorless liquid (93%, 48 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.28−7.23 (m, 1H), 7.15 (dd, J = 7.6, 0.8 Hz, 1H), 7.05 (td, J = 7.6, 0.8 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.21 (s, 3H), 1.93 (dd, J = 14.0, 6.8 Hz, 1H), 1.72 (dd, J = 14.0, 4.8 Hz, 1H), 1.48−1.44 (m, 3H), 1.31−1.21 (m, 5H), 0.98−0.83 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.1, 143.1, 134.4, 127.5, 122.7, 122.3, 107.9, 47.8, 45.4, 34.7, 34.4, 33.5, 26.2, 26.1, 26.0 ppm.

*3-Cyclohexylmethyl-1,3,5-trimethylindolin-2-one (**3b**).*[7d] Colorless liquid (79%, 43 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, J = 7.6 Hz, 1H), 6.96 (s, 1H), 6.71 (d, J = 7.6 Hz, 1H), 3.18 (s, 3H), 2.34 (s, 3H), 1.90 (dd, J = 14.0, 6.8 Hz, 1H), 1.69 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.45 (m, 3H), 1.35−1.20 (m, 5H), 1.00−0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.1, 140.7, 134.4, 131.7, 127.7, 123.5, 107.6, 47.8, 45.4, 34.6, 34.4, 33.4, 26.2, 26.1, 26.0, 21.2 ppm.

*3-Cyclohexylmethyl-5-methoxy-1,3-dimethylindolin-2-one (**3c**).*[7d] Colorless liquid (87%, 50 mg); R_f 0.2 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$): δ = 6.79−6.72 (m, 3H), 3.80 (s, 3H), 3.18 (s, 3H), 1.91 (dd, J = 14.0, 6.8 Hz, 1H), 1.68 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.45 (m, 3H), 1.34−1.19 (m, 5H), 1.01−0.73 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.7, 155.8, 136.6, 135.8, 111.3, 110.4, 108.1, 55.7, 48.2, 45.3, 34.7, 34.4, 33.4, 26.3, 26.2, 26.0 ppm.

*3-Cyclohexylmethyl-5-trifluoromethyl-1,3-dimethylindolin-2-one (**3d**).* Colorless liquid (91%, 54 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.54 (dd, J = 8.0, 0.8 Hz, 1H), 7.37 (t, J = 0.8 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 3.24 (s, 3H), 1.95 (dd, J = 14.0, 6.8 Hz, 1H), 1.75 (dd, J = 14.0, 5.2 Hz, 1H), 1.51−1.45 (m, 3H), 1.33 (s, 3H), 1.29−1.16 (m, 2H), 1.01−0.69 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.0, 146.0, 135.0, 125.4

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(q, J = 4.0 Hz), 124.5 (q, J = 32.2 Hz), 124.4 (q, J = 269.9 Hz), 119.6 (q, J = 3.6 Hz), 107.7, 47.8, 45.2, 34.7, 34.3, 33.4, 26.4, 26.0, 25.9 ppm; IR (KBr): υ_{max} 2926, 2852, 1724, 1621, 1455, 1330, 1287, 1122 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}F_3NNaO$ $[M + Na]^+$ 348.1546, found 348.1537.

*3-Cyclohexylmethyl-1,3-dimethyl-2-oxo-2,3-dihydro-1H-indole-5-carbonitrile (**3e**).* White solid, mp = 113−115 °C (80%, 45 mg); R_f 0.1 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (dd, J = 8.0, 1.6 Hz, 1H), 7.39 (d, J = 1.6 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 3.24 (s, 3H), 1.95 (dd, J = 14.4, 6.8 Hz, 1H), 1.73 (dd, J = 14.0, 4.8 Hz, 1H), 1.51−1.46 (m, 3H), 1.31 (s, 3H), 1.27−1.16 (m, 2H), 1.01−0.73 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.7, 146.9, 135.4, 133.0, 126.0, 119.4, 108.4, 105.4, 47.6, 45.1, 34.7, 34.4, 33.3, 26.4, 26.0, 25.9 ppm; IR (KBr): υ_{max} 2924, 2851, 2222, 1724, 1614, 1496, 1338 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}N_2NaO$ $[M + Na]^+$ 305.1624, found 305.1621.

*3-Cyclohexylmethyl-1,3-dimethyl-2-oxo-2,3-dihydro-1H-indole-5-carboxylic Acid Ethyl Ester (**3f**).* Colorless liquid (88%, 55 mg); R_f 0.2 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (dd, J = 8.0, 1.6 Hz, 1H), 7.81 (d, J = 1.6 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 4.39−4.34 (m, 2H), 3.23 (s, 3H), 1.93 (dd, J = 14.4, 7.2 Hz, 1H), 1.77 (dd, J = 14.0, 4.8 Hz, 1H), 1.50−1.38 (m, 6H), 1.32−1.17 (m, 5H), 1.01−0.73 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.4, 166.6, 147.1, 134.3, 130.3, 124.6, 123.9, 107.4, 60.9, 47.6, 45.2, 34.7, 34.3, 33.3, 26.4, 26.1, 26.0, 25.9, 14.4 ppm; IR (KBr): υ_{max} 2923, 1716, 1614, 1455, 1274, 1105, 769 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{27}NNaO_3$ $[M + Na]^+$ 352.1883, found 352.1875.

*5-Chloro-3-cyclohexylmethyl-1,3-dimethylindolin-2-one (**3g**).*[7d] Colorless liquid (76%, 44 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (dd, J = 8.4, 2.0 Hz, 1H), 7.12 (d, J = 2.0 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 3.20 (s, 3H), 1.93 (dd, J = 14.0, 6.8 Hz, 1H), 1.69 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.47 (m, 3H), 1.32−1.20 (m, 5H), 1.03−0.77 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.6, 141.7, 136.2, 127.8, 127.5, 123.2, 108.9, 48.1, 45.3, 34.7, 34.4, 33.4, 26.3, 26.2, 26.0 ppm.

*3-Cyclohexylmethyl-1,3,7-trimethylindolin-2-one (**3i**).*[7d] Colorless liquid (71%, 38 mg); R_f 0.4 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97−6.89 (m, 3H), 3.48 (s, 3H), 2.57 (s, 3H), 1.90 (dd, J = 14.0, 6.8 Hz, 1H), 1.67 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.44 (m, 3H), 1.36−1.18 (m, 5H), 0.99−0.69 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.7, 140.7, 134.9, 131.1, 122.1, 120.5, 119.4, 47.0, 45.5, 34.5, 34.4, 33.4, 29.4, 26.5, 26.0, 25.9, 19.0 ppm.

*3-Cyclohexylmethyl-7-methoxy-1,3-dimethylindolin-2-one (**3j**).*[7d] Colorless liquid (79%, 45 mg); R_f 0.2 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (t, J = 8.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 7.6 Hz, 1H), 3.84 (s, 3H), 3.47 (s, 3H), 1.89 (dd, J = 14.0, 6.8 Hz, 1H), 1.67 (dd, J = 14.0, 4.8 Hz, 1H), 1.51−1.44 (m, 3H), 1.37−1.19 (m, 5H), 0.98−0.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.3, 145.2, 136.0, 130.7, 122.7, 115.4, 111.2, 55.7, 47.8, 45.4, 34.6, 34.4, 33.4, 29.4, 26.4, 26.0, 25.9 ppm.

*3-Cyclohexylmethyl-7-fluoro-1,3-dimethylindolin-2-one (**3k**).*[7d] Colorless liquid (80%, 43.8 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99−6.92 (m, 3H), 3.42 (d, J = 2.4 Hz, 3H), 1.92 (dd, J = 14.0, 6.8 Hz, 1H), 1.70 (dd, J = 14.0, 5.2 Hz, 1H), 1.53−1.47 (m, 3H), 1.36−1.19 (m, 5H), 1.01−0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.7, 147.7 (d, J = 241.8 Hz), 137.4 (d, J = 2.9 Hz), 129.6 (d, J = 7.7 Hz), 122.8 (d, J = 6.3 Hz), 118.5 (d, J = 3.1 Hz), 115.5 (d, J = 19.1 Hz), 48.2 (d, J = 1.6 Hz), 45.5, 34.7, 34.4, 33.4, 26.4, 28.6, 26.1, 26.0 ppm.

*3-Cyclohexylmethyl-1,3-dimethyl-7-phenylindolin-2-one (**3l**).* White solid, mp = 90−92 °C (82%, 55 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43−7.31 (m, 5H), 7.15 (dd, J = 6.8, 2.0 Hz, 1H), 7.10−7.04 (m, 2H), 2.73 (s, 3H), 1.96 (dd, J = 14.0, 7.2 Hz, 1H), 1.75 (dd, J = 14.0, 5.2 Hz, 1H), 1.56−1.50 (m, 3H), 1.42−1.23 (m, 5H), 1.02−0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.2, 140.1, 139.2, 135.4, 130.5, 129.9, 127.8, 127.5, 125.3, 121.7, 121.6, 47.1, 45.9, 34.8, 34.5, 33.6, 30.1, 26.2, 26.1 ppm; IR (KBr): υ_{max} 2922, 1769, 1716, 1455, 1372, 1245, 1061 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{28}NO$ $[M + H]^+$ 334.2165, found 334.2160.

*3-Cyclohexylmethyl-1,3,6,7-tetramethylindolin-2-one (**3m**).* Colorless liquid (40%, 23 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88−6.84 (m, 2H), 3.51 (s, 3H), 2.48 (s, 3H), 2.30 (s, 3H), 1.89 (dd, J = 14.0, 6.8 Hz, 1H), 1.66 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.45 (m, 3H), 1.36−1.20 (m, 5H), 1.00−0.69 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.4, 141.1, 137.1, 132.9, 123.9, 119.9, 118.7, 46.8, 45.6, 34.5, 34.4, 33.4, 30.4, 26.8, 26.1, 26.0, 25.9, 20.9, 14.2 ppm; IR (KBr): υ_{max} 2922, 2851, 1712, 1608, 1451, 1363, 1057 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{27}NNaO$ $[M + Na]^+$ 308.1985, found 308.1976.

*3-Cyclohexylmethyl-5,7-dimethoxy-1,3-dimethylindolin-2-one (**3n**).*[7d] Colorless liquid (65%, 52 mg); R_f 0.2 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.38 (s, 1H), 6.33 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.40 (s, 3H), 1.86 (dd, J = 14.0, 6.8 Hz, 1H), 1.61 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.43 (m, 3H), 1.36−1.20 (m, 5H), 0.96−0.67 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.9, 156.4, 145.7, 136.7, 124.3, 100.6, 98.5, 55.7, 48.3, 45.4, 34.5, 34.3, 33.3, 29.2, 26.5, 26.0, 25.9 ppm.

*3-Cyclohexylmethyl-1,3,4,6-tetramethylindolin-2-one (**3o**).*[7d] Colorless liquid (76%, 43.3 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.63 (s, 1H), 6.51 (s, 1H), 3.17 (s, 3H), 2.33 (s, 3H), 2.29 (s, 3H), 1.92 (s, 2H), 1.49−1.21 (m, 8H), 0.98−0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.5, 143.3, 137.2, 133.8, 127.9, 125.4, 106.7, 48.4, 43.8, 35.1, 34.1, 32.9, 26.2, 26.0, 25.9, 24.1, 21.5, 18.1 ppm.

*1-Benzyl-3-cyclohexylmethyl-3-methylindolin-2-one (**3p**).*[7d] White solid (83%, 55 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31−7.24 (m, 5H), 7.17−7.12 (m, 2H), 7.02 (t, J = 7.6 Hz, 1H), 6.74 (d, J = 7.6 Hz, 1H), 5.05 (d, J = 15.6 Hz, 1H), 4.80 (d, J = 15.6 Hz, 1H), 1.99 (dd, J = 14.0, 6.4 Hz, 1H), 1.76 (dd, J = 14.0, 5.6 Hz, 1H), 1.51−1.42 (m, 4H), 1.37 (s, 3H), 1.16−1.13 (m, 1H), 1.04−0.80 (m, 5H), 0.75−0.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.0, 142.2, 136.1, 134.5, 128.7, 127.5, 127.4, 122.7, 122.3, 109.0, 47.9, 45.4, 43.7, 34.8, 34.3, 33.9, 26.6, 26.1, 26.0 ppm.

*3-Cyclohexylmethyl-3-methyl-1-phenylindolin-2-one (**3q**).*[7d] White solid (80%, 51 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (t, J = 8.4 Hz, 2H), 7.42−7.38 (m, 3H), 7.25−7.18 (m, 2H), 7.10 (t, J = 7.2 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H), 2.06 (dd, J = 14.0, 7.2 Hz, 1H), 1.83 (dd, J = 14.0, 5.2 Hz, 1H), 1.58−1.52 (m, 4H), 1.46 (s, 3H), 1.32−1.28 (m, 1H), 1.16−0.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.3, 142.9, 134.7, 134.1, 129.5, 127.7, 127.3, 126.4, 122.9, 122.7, 109.2, 47.8, 45.8, 34.9, 34.3, 33.5, 26.4, 26.1, 26.0 ppm.

*3-Benzyl-3-cyclohexylmethyl-1-methylindolin-2-one (**3r**).* White solid, mp = 68−70 °C (81%, 54 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18−7.13 (m, 2H), 7.05−6.98 (m, 4H), 6.74 (dd, J = 7.6, 1.2 Hz, 2H), 6.54 (d, J = 7.6 Hz, 1H), 3.07 (d, J = 12.4 Hz, 1H), 2.92 (d, J = 12.8 Hz, 1H), 2.90 (s, 3H), 2.08 (dd, J = 14.0, 7.2 Hz, 1H), 1.88 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.45 (m, 3H), 1.36−1.23 (m, 2H), 1.06−0.73 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5, 143.6, 135.6, 131.3, 129.8, 127.6, 127.2, 126.3, 123.7, 121.8, 107.6, 54.1, 46.2, 43.8, 34.7, 34.5, 33.4, 26.1, 26.0, 25.8 ppm; IR (KBr): υ_{max} 2921, 2850, 1712, 1612, 1493, 1469, 1377, 1343, 1088, 751, 700 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{27}NNaO$ $[M + Na]^+$ 356.1985, found 356.1979.

*3-Cyclohexylmethyl-1-methyl-3-phenylindolin-2-one (**3s**).* White solid, mp = 62−64 °C (82%, 52 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38−7.31 (m, 3H), 7.28−7.20 (m, 4H), 7.12 (td, J = 7.6, 0.8 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 3.20 (s, 3H), 2.41 (dd, J = 14.0, 7.2 Hz, 1H), 2.15 (dd, J = 14.0, 5.2 Hz, 1H), 1.54−1.25 (m, 5H), 1.06−0.85 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.9, 143.8, 141.5, 131.9, 128.3, 128.0, 127.0, 126.6, 125.2, 122.3, 108.2, 55.9, 45.2, 34.8, 34.5, 33.5, 26.4, 26.1, 26.0 ppm; IR (KBr): υ_{max} 2922, 1764, 1715, 1609, 1461, 1376, 1244, 1061 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{25}NNaO$ $[M + Na]^+$ 342.1828, found 342.1825.

*3-Cyclohexylmethyl-3-hydroxymethyl-1,5-dimethylindolin-2-one (**3t**).* White solid, mp = 121−123 °C (35%, 20 mg); R_f 0.2 (EtOAc/petroleum ether = 1:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10

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(d, J = 7.6 Hz, 1H), 6.98 (s, 1H), 6.76 (d, J = 7.6 Hz, 1H), 3.75 (d, J = 10.0 Hz, 1H), 3.60 (dd, J = 10.4, 2.4 Hz, 1H), 3.21 (s, 3H), 2.36 (s, 3H), 2.29 (dd, J = 8.8, 3.2 Hz, 1H), 2.05 (dd, J = 14.0, 7.6 Hz, 1H), 1.73 (dd, J = 14.0, 5.2 Hz, 1H), 1.52−1.46 (m, 3H), 1.33−1.23 (m, 2H), 1.03−0.93 (m, 4H), 0.84−0.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.6, 141.6, 132.1, 130.2, 128.5, 123.9, 108.0, 68.8, 53.9, 39.9, 34.4, 34.2, 33.3, 26.2, 26.0, 25.9, 21.2 ppm; IR (KBr): υ_{max} 2923, 2855, 1703, 1612, 1498, 1454, 1359, 1247, 1069 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{25}NNaO_2$ [M + Na]$^+$ 310.1777, found 310.1763.

General Procedure for the Cyclization of Acrylamides with Secondary Alkyl Bromides. Acrylamides **1** (0.2 mmol, 1.0 equiv), $PdCl_2$ (3.4 mg, 10 mol %), dppf (11.8 mg, 10 mol %), $K_3PO_4{\cdot}3H_2O$ (106 mg, 0.4 mmol, 2.0 equiv), and NaI (89.4 mg, 0.6 mmol, 3.0 equiv) were added into an oven-dried sealed tube. The tube was evacuated and backfilled with nitrogen (three times). Then, a solution of alkyl bromides **2** (0.5 mmol, 2.5 equiv) in diglyme (2.0 mL) was injected into the tube by syringe. The tube was then sealed with a Teflon lined cap, and the mixture was stirred at 100 °C for 24 h. The resulting mixture was diluted with EtOAc, and the organic phase was washed successively with H_2O (three times) and brine (one time), then dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc/petroleum ether: 1/20 to 1/10) to give the corresponding products **4** in yields listed in Table 3.

General Procedure for the Cyclization of Acrylamides with Tertiary Alkyl Bromides and Benzyl Bromides. Acrylamides **1** (0.2 mmol, 1.0 equiv), $PdCl_2$ (3.4 mg, 10 mol %), dppf (11.8 mg, 10 mol %), and $K_3PO_4{\cdot}3H_2O$ (106 mg, 0.4 mmol, 2.0 equiv) were added into an oven-dried sealed tube. The tube was evacuated and backfilled with nitrogen (three times). Then, a solution of tertiary alkyl bromides or benzyl bromides **2** (0.5 mmol, 2.5 equiv) in diglyme (2.0 mL) was injected into the tube by syringe. The tube was then sealed with a Teflon lined cap, and the mixture was stirred at 100 °C for 24 h. The resulting mixture was diluted with EtOAc, and the organic phase was washed successively with H_2O (three times) and brine (one time), then dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc/petroleum ether: 1/20 to 1/10) to give the corresponding products **4** in yields listed in Table 3.

*3-Cyclopentylmethyl-1,3-dimethylindolin-2-one (**4a**).*[7d] Colorless liquid (86%, 42 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27−7.23 (m, 1H), 7.15 (dd, J = 7.2, 0.8 Hz, 1H), 7.04 (td, J = 7.6, 0.8 Hz, 1H), 6.83 (d, J = 7.6 Hz, 1H), 3.20 (s, 3H), 2.05 (dd, J = 13.6, 7.2 Hz, 1H), 1.88 (dd, J = 14.0, 6.0 Hz, 1H), 1.51−1.36 (m, 3H), 1.33 (s, 3H), 1.31−1.20 (m, 4H), 1.04−0.95 (m, 1H), 0.87−0.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.0, 143.2, 134.3, 127.5, 122.8, 122.2, 107.8, 48.4, 44.4, 37.1, 33.7, 32.7, 26.1, 25.2, 24.9, 24.8 ppm.

*1,3-Dimethyl-3-(2-methyl-octyl)indolin-2-one (**4b**).* Colorless liquid (55%, 31.6 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); The mixture of isomers cannot be separated by column chromatography on silica gel. The NMR spectroscopy of mixture (d.r. = 1:1), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28−7.23 (m, 1H), 7.18−7.13 (m, 1H), 7.07−7.03 (m, 1H), 6.84 (dd, J = 8.0, 4.0 Hz, 1H), 3.21 (s, 3H), 2.01 (dd, J = 14.0, 5.6 Hz, 0.5H), 1.85 (d, J = 6.0 Hz, 1H), 1.66 (dd, J = 14.0, 6.4 Hz, 0.5H), 1.32 (s, 3H), 1.23−0.87 (m, 11H), 0.84 (t, J = 7.2, 2.4 Hz, 3H), 0.60 (d, J = 6.4 Hz, 1.5H), 0.50 (d, J = 6.8 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.3, 180.9, 143.2, 134.5, 134.1, 127.5, 122.9, 122.8, 122.3, 122.2, 107.9, 48.1, 47.9, 45.5, 44.8, 38.1, 37.2, 31.7, 30.1, 29.9, 29.3, 26.5, 26.4, 26.2, 26.1, 25.8, 22.6, 20.8, 19.9, 14.1 ppm; IR (KBr): υ_{max} 2930, 1717, 1611, 1463, 1376, 1344, 1125, 749 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{30}NO$ [M + H]$^+$ 288.2322, found 288.2319.

*1,3-Dimethyl-3-pentylindolin-2-one (**4c**).* Colorless liquid (39%, 18 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28−7.24 (m, 1H), 7.17 (dd, J = 7.2, 0.8 Hz, 1H), 7.06 (td, J = 7.6, 0.8 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.21 (s, 3H), 1.88 (td, J = 13.2, 4.8 Hz, 1H), 1.72 (td, J = 13.2, 4.0 Hz, 1H), 1.35 (s, 3H), 1.18−1.08 (m, 4H), 1.03−0.76 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.8, 143.2, 134.2, 127.5, 122.3, 107.8, 48.3, 38.4, 31.8, 26.0, 24.0, 23.7, 22.2, 13.9 ppm; IR (KBr): υ_{max} 2928, 1714, 1612, 1464, 1376, 1346, 1252, 1126, 1087, 1024, 750 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NNaO$ [M + Na]$^+$ 254.1515, found 254.1516.

*1,3-Dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoro-pentyl)indolin-2-one (**4d**).*[7f] Colorless liquid (76%, 60 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33−7.27 (m, 2H), 7.08 (td, J = 7.6, 0.8 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 3.24 (s, 3H), 2.94−2.53 (m, 2H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.5, 142.8, 131.2, 128.5, 123.5, 122.6, 120.2−112.2 (m), 108.4, 44.2, 36.9 (t, J = 20.2 Hz), 29.7, 26.4, 25.8 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) −81.2 (t, J = 7.5 Hz, 3F), −109.0 (m, 1F), −114.6 (m, 1F), −124.7 (m, 2F), −126.0 (m, 2F).

*1,3-Dimethyl-3-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-heptyl)-indolin-2-one (**4e**).* Colorless liquid (65%, 64 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34−7.27 (m, 2H), 7.09 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 3.25 (s, 3H), 2.95−2.54 (m, 2H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.6, 142.8, 131.2, 128.5, 123.6, 122.6, 120.0−110.1 (m), 108.5, 44.2, 37.0 (t, J = 19.4 Hz), 26.4, 25.9 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) −80.9 (t, J = 11.3 Hz, 3F), −108.7 (m, 1F), −114.5 (m, 1F), −121.8 (m, 2F), −123.0 (m, 2F), −123.7 (m, 2F), −126.2 (m, 2F); IR (KBr): υ_{max} 2931, 1722, 1615, 1495, 1474, 1351, 1240, 1144, 1050 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{12}F_{13}NNaO$ [M + Na]$^+$ 516.0603, found 516.0605.

*3-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-Heptadecafluoro-nonyl)-1,3-dimethylindolin-2-one (**4f**).* Colorless liquid (68%, 81 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33−7.28 (m, 2H), 7.11−7.07 (m, 1H), 6.90 (d, J = 7.6 Hz, 1H), 3.25 (s, 3H), 2.97−2.55 (m, 2H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.6, 142.8, 131.3, 128.4, 123.5, 122.6, 120.2−107.5 (m), 44.2, 37.0 (t, J = 20.3 Hz), 26.3, 25.8 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) −81.1 (t, J = 11.3 Hz, 3F), −108.8 (m, 1F), −114.5 (m, 1F), −121.7 (m, 2F), −122.2 (m, 4F), −123.0 (m, 2F), −123.8 (m, 2F), −126.4 (m, 2F); IR (KBr): υ_{max} 3061, 2975, 1720, 1616, 1495, 1474, 1427, 1351, 1207, 1080, 1051, 1026 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{13}F_{17}NO$ [M + H]$^+$ 594.0720, found 594.0734.

*3-Cycloheptylmethyl-1,3-dimethylindolin-2-one (**4g**).*[7d] Colorless liquid (70%, 38 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27−7.24 (m, 1H), 7.16 (dd, J = 7.2, 0.8 Hz, 1H), 7.07−7.03 (m, 1H), 6.84 (d, J = 8.0 Hz, 1H), 3.21 (s, 3H), 1.99 (dd, J = 13.6, 6.8 Hz, 1H), 1.75 (dd, J = 14.0, 4.4 Hz, 1H), 1.43−1.32 (m, 10H), 1.18−0.97 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.0, 143.1, 134.2, 127.4, 122.7, 122.2, 107.8, 48.1, 45.9, 36.1, 35.8, 34.4, 28.4, 26.1, 25.8, 25.7 ppm.

*1,3-Dimethyl-3-(2-methyl-butyl)indolin-2-one (**4h**).* Colorless liquid (76%, 34 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10). The mixture of isomers cannot be separated by column chromatography on silica gel. The NMR spectroscopy of mixture (d.r. = 1:1), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26−7.22 (m, 1H), 7.17−7.12 (m, 1H), 7.06−7.02 (m, 1H), 6.84−6.81 (m, 1H), 3.20 (s, 3H), 2.01 (dd, J = 14.0, 5.2 Hz, 0.5H), 1.85 (d, J = 5.6 Hz, 1H), 1.64 (dd, J = 14.0, 6.4 Hz, 0.5H), 1.31 (s, 3H), 1.17−0.90 (m, 3H), 0.70 (q, J = 6.8 Hz, 3H), 0.58 (d, J = 6.4 Hz, 1.5H), 0.47 (d, J = 6.8 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.2, 180.8, 143.1, 134.5, 133.9, 127.5, 122.8, 122.7, 122.2, 107.8, 48.1, 47.8, 44.9, 44.3, 31.5, 30.6, 30.0, 26.1, 26.0, 25.7, 20.2, 19.2, 11.0, 10.9 ppm; IR (KBr): υ_{max} 2962, 2926, 1717, 1613, 1492, 1469, 1376, 1346, 1247, 1123, 1087, 1022 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NNaO$ [M + Na]$^+$ 254.1515, found 254.1513.

*3-(2,2-Dimethyl-propyl)-1,3-dimethylindolin-2-one (**4i**).*[7g] White solid, (40%, 14 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26−7.23 (m, 1H), 7.19 (dd, J = 7.6, 0.8 Hz, 1H), 7.02 (td, J = 7.2, 0.8 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.21 (s, 3H), 2.15 (d, J = 14.4 Hz, 1H), 1.85 (d, J = 14.4 Hz, 1H), 1.29 (s, 3H), 0.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.0, 142.8, 134.2, 127.5, 123.8, 121.9, 108.0, 50.8, 47.4, 31.7, 30.8, 28.2, 26.2 ppm.

*3-Adamantan-1-ylmethyl-1,3-dimethylindolin-2-one (**4j**).*[7g] White solid, (31%, 19 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28−7.24 (m, 1H), 7.19 (d,

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J = 7.2 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 3.23 (s, 3H), 2.00 (d, J = 14.4 Hz, 1H), 1.75−1.69 (m, 4H), 1.52−1.49 (m, 3H), 1.39−1.36 (m, 3H), 1.27 (s, 3H), 1.21−1.13 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.2, 142.6, 134.7, 127.5, 123.6, 122.0, 108.0, 52.0, 46.6, 43.3, 36.7, 33.9, 28.6, 28.5, 26.3 ppm.

*1,3-Dimethyl-3-phenethylindolin-2-one (**4k**).*[10c] White solid (62%, 33 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (t, J = 7.6 Hz, 1H), 7.25−7.20 (m, 3H), 7.16−7.10 (m, 2H), 7.04 (d, J = 7.2 Hz, 2H), 6.87 (d, J = 8.0 Hz, 1H), 3.22 (s, 3H), 2.36−2.25 (m, 2H), 2.18−1.99 (m, 2H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.2, 143.3, 141.3, 133.7, 128.2, 128.1, 127.8, 125.8, 122.5, 122.4, 107.9, 48.3, 40.2, 30.9, 26.0, 23.9 ppm.

*1,3-Dimethyl-3-(2-p-tolyl-ethyl)indolin-2-one(**4l**).*[10c] White solid (60%, 33 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 7.2 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.6 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 7.6 Hz, 1H), 3.22 (s, 3H), 2.29−2.22 (m, 5H), 2.13−1.97 (m, 2H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.3, 143.4, 138.3, 135.2, 133.7, 128.9, 128.1, 127.7, 122.5, 122.4, 107.9, 48.3, 40.4, 30.4, 26.1, 23.9, 20.9 ppm.

*4-[2-(1,3-Dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-ethyl]-benzonitrile (**4m**).*[10c] White solid (77%, 47 mg); R_f 0.3 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, J = 8.0 Hz, 2H), 7.31 (td, J = 7.2, 0.8 Hz, 1H), 7.22 (d, J = 6.8 Hz, 1H), 7.12−7.09 (m, 3H), 6.89 (d, J = 7.6 Hz, 1H), 3.20 (s, 3H), 2.38−2.19 (m, 3H), 2.06−2.00 (m, 1H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.7, 146.8, 143.1, 133.0, 131.8, 128.9, 127.9, 122.5, 122.2, 118.7, 109.5, 108.0, 48.0, 39.1, 31.0, 25.9, 23.8 ppm.

*4-[2-(1,3-Dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-ethyl]-benzoic Acid Methyl Ester (**4n**).* White solid, mp = 67−69 °C (79%, 51 mg); R_f 0.4 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.4 Hz, 2H), 7.30 (td, J = 7.6, 0.8 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.11 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 7.6 Hz, 1H), 3.87 (s, 3H), 3.19 (s, 3H), 2.37−2.16 (m, 3H), 2.05−1.98 (m, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.1, 167.0, 146.8, 143.3, 133.4, 129.5, 128.3, 127.9, 127.8, 122.6, 122.4, 108.1, 51.9, 48.3, 39.6, 31.0, 26.1, 23.9 ppm; IR (KBr): υ_{max} 2939, 1716, 1611, 1464, 1443, 1376, 1346, 1280, 1184, 1107, 757 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}NNaO_3$ $[M + Na]^+$ 346.1414, found 346.1413.

*3-[2-(2,6-Dichloro-phenyl)-ethyl]-1,3-dimethylindolin-2-one (**4o**).* White solid, mp = 70−72 °C (78%, 52 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31−7.28 (m, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.10 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 3.26 (s, 3H), 2.65 (td, J = 12.8, 4.8 Hz, 1H), 2.45 (td, J = 12.8, 4.4 Hz, 1H), 2.16 (td, J = 12.8, 4.8 Hz, 1H), 1.94 (td, J = 13.2, 4.4 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.9, 143.3, 137.2, 135.1, 133.3, 128.0, 127.9, 127.6, 122.7, 122.4, 107.9, 48.1, 35.7, 26.6, 26.2, 23.6 ppm; IR (KBr): υ_{max} 2927, 1714, 1611, 1442, 1346, 1250, 1128, 764 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{18}Cl_2NO$ $[M + H]^+$ 334.0760, found 334.0747.

General Procedure for the Cyclization of Cinnamamide with Iodocyclohexane 2a. Cinnamamide **5a** (0.2 mmol, 1.0 equiv), $PdCl_2$ (3.4 mg, 10 mol %), dppf (11.8 mg, 10 mol %), and $K_3PO_4{\cdot}3H_2O$ (106 mg, 0.4 mmol, 2.0 equiv) were added into an oven-dried sealed tube. The tube was evacuated and backfilled with nitrogen (three times). Then, a solution of iodocyclohexane **2a** (0.5 mmol, 2.5 equiv) in diglyme (2.0 mL) was injected into the tube by syringe. The tube was then sealed with a Teflon lined cap, and the mixture was stirred at 100 °C for 24 h. The resulting mixture was diluted with EtOAc, and the organic phase was washed successively with H_2O (three times) and brine (one time), then dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc/petroleum ether: 1/20 to 1/10) to give the corresponding product **6a** in 39% yield (25 mg).

*3-Cyclohexylmethyl-1-methyl-4-phenyl-3,4-dihydro-1H-quinolin-2-one (**6a**).*[10f] Colorless liquid; R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (td, J = 8.0, 1.2 Hz, 1H), 7.24−7.13 (m, 4H), 7.07 (d, J = 7.2 Hz, 2H), 6.97 (d, J = 7.2 Hz, 2H), 4.22 (s, 1H), 3.37 (s, 3H), 2.68 (dd, J = 8.8, 1.6 Hz, 1H), 1.94−1.92 (m, 1H), 1.71−1.68 (m, 2H), 1.60−1.58 (m, 2H), 1.40−1.37 (m, 1H), 1.30−1.21 (m, 1H), 1.13−1.05 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 142.3, 140.0, 129.6, 128.6, 128.0, 127.0, 126.6, 123.2, 114.8, 55.6, 44.4, 37.7, 31.3, 31.1, 29.4, 26.1, 26.0 ppm.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02433.

^{1}H and ^{13}C spectra of all new compounds; the primary mechanistic and KIE studies of the reactions (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: duanxh@mail.xjtu.edu.cn.

Notes

The authors declare no competing financial interest.

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