Synthesis C.-P. Chuang et al. Paper

Copper-Salt-Promoted Carbocyclization Reactions of α-Bromo-*N*-arylacylamides

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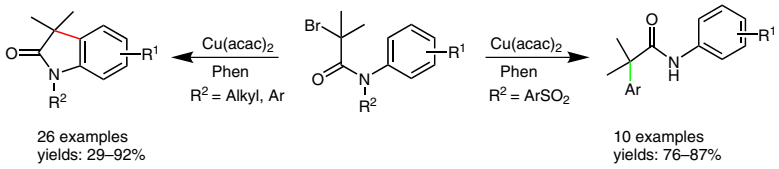


Received: 05.09.2016
Accepted after revision: 11.10.2016
Published online: 07.11.2016
DOI: 10.1055/s-0036-1588642; Art ID: ss-2016-f0606-op

Abstract A mild and convenient synthetic method for oxindoles and α-arylacylamides bearing an all carbon quaternary stereocenter from the readily available α-bromo-*N*-arylacylamides has been developed. This Cu(acac)$_2$/Phen-promoted radical cyclization reaction, via the intramolecular radical cyclization onto the aryl moiety, can proceed in two different routes depending on the substituents on the nitrogen atom. In this transformation, oxindoles and α-arylacylamides were formed in high chemoselectivity. A variety of useful functional groups such as methoxy, fluoro, chloro, bromo, methoxycarbonyl, and cyano are compatible with the reaction conditions. The use of inexpensive, readily available Cu(acac)$_2$ and Phen makes this protocol very efficient and practical.

Key words copper salts, carbocyclization, α-bromo-*N*-arylacylamides, oxindoles, α-arylacylamides

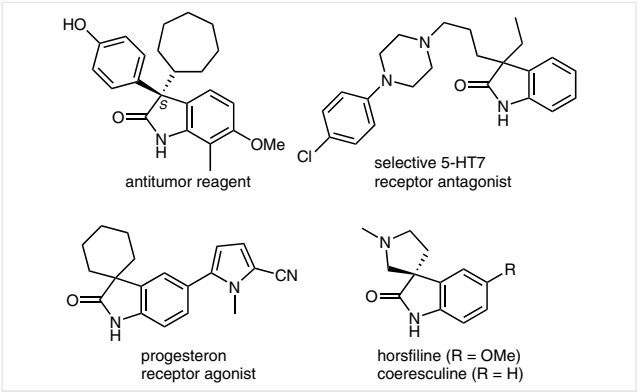
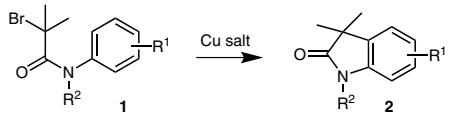


Figure 1 Several biologically active oxindole derivatives[2]

3,3′-Disubstituted oxindoles are an important class of nitrogen heterocycles found in a wide range of natural products and bioactive molecules (Figure 1).[1,2] Owing to their significance of biological activities and a wide range of applications in organic synthesis, they become attractive targets in organic synthesis. Therefore, numerous methods for the synthesis of these motifs have been established, including Pd-catalyzed cyclization reactions of *N*-(*o*-haloaryl)amides (Mizoroki–Heck couplings[3] and arylations[4]), base-promoted cyclization reactions of α-activated-*N*-arylamides,[5] radical cyclization reactions of *N*-arylamides,[6,7] and tandem radical addition-cyclization reactions of *N*-arylacrylamides.[8]

Copper-promoted atom-transfer radical cyclization reaction (ATRC) has been extensively studied and is widely used in the preparation of carbocycles and heterocyles.[9] Recently, their analogous reactions using alkyl bromides as radical precursors have been developed as a powerful tool for the tertiary alkenylation of α-carbonyl alkyl bromides without either β-hydrogen elimination or oxidative addition, which are problematic in Mizoroki–Heck couplings.[10,11] The copper-promoted cyclization reactions have received considerable attention because of their efficiencies, low-costs, and good functional group tolerances in the substrates. Many useful N-heterocyclic compounds such as pyrroles,[12] indoles,[13] oxazoles,[14] pyrazoles,[15] and quinolines[16] have been efficiently synthesized by these methods.

Although a number of effective methods for the syntheses of 3,3′-disubstituted oxindoles are available, the exploration of mild and efficient methods is continuously being pursued. As part of our research interest in developing new methods for the preparation of heterocyclic systems,[17–21] we now report a mild method for the synthesis of 3,3′-disubstituted oxindoles through the copper salts-promoted radical cyclizations of α-bromo-*N*-arylacylamides (Scheme 1).

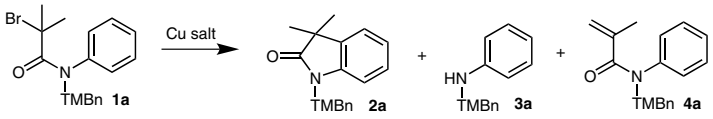


Scheme 1 Cyclization of α-bromo-*N*-arylacylamides

In our initial experiment, α-bromo-*N*-arylacylamide **1a** [R^1 = H, R^2 = 2,4,6-trimethylbenzyl (TMBn)] was treated with $Cu(acac)_2$ (0.5 equiv), and 1,10-phenanthroline (Phen) (0.5 equiv) in DMF at 90 °C under a nitrogen atmosphere for 8 hours (Table 1, entry 1). The 3,3′-disubstituted oxindole **2a**, formed via the five-membered-ring cyclization of carbamoylmethyl radical **I** (Scheme 2), was produced in 77% yield and another unexpected *N*-benzylaniline **3a** was also obtained in 12% yield. The reaction yield of **2a** can be improved to 90% by increasing the amount of $Cu(acac)_2$ and Phen up to 2 equivalents and the reaction time was shorten to 6 hours (entry 3). In this transformation, *N*-arylacrylamide **4a**, derived from the β-hydrogen elimination, was not observed. Several other inexpensive, readily available copper salts were next tested, the results showed that $Cu(acac)_2$ and Cu_2O were more efficient than the others.

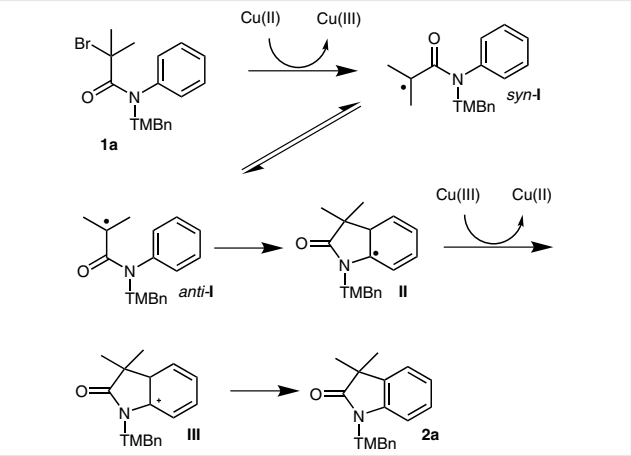
The effect of solvent was also investigated, and the results revealed that DMF and EtCN were the most suitable solvents for this reaction (Table 1, entries 3, 8–12). Notably, the addition of ligand is crucial for the success of this reaction. Compared to Phen, other pyridine ligands such as 2,2′-bipyridine and pyridine are less efficient (entries 14 and 15). In the absence of Phen, product **2a** could not be found and the starting **1a** was recovered (85%) after heating for 6 hours at 90 °C (entry 16). In addition, the temperature has an obvious influence on this reaction, thus reaction at 90 °C provided **2a** in high yield (entries 12, 17, and 18). We also performed this reaction under air atmosphere. After heating for 6 hours, the target product **2a** was obtained in 83%

Table 1 Optimization of Reaction Conditions for the Copper-Promoted Carbocyclization Reactions with α-Bromo-*N*-arylacylamides **1a**



Entry	Cu salt (equiv)	Ligand (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[a]	
1	$Cu(acac)_2$ (0.5)	Phen (0.5)	DMF	90	8	**2a** (77)	**3a** (12)
2	$Cu(acac)_2$ (0.5)	Phen (2)	DMF	90	8	**2a** (73)	**3a** (11)
3	$Cu(acac)_2$ (1)	Phen (1)	DMF	90	6	**2a** (82)	**3a** (7)
4	$Cu(acac)_2$ (2)	Phen (2)	DMF	90	6	**2a** (90)	
5	Cu_2O (1)	Phen (2)	DMF	90	6	**2a** (90)	
6	CuCl (2)	Phen (2)	DMF	90	6	**2a** (61)	
7	CuBr (2)	Phen (2)	DMF	90	6	**2a** (0)	
8	$Cu(OAc)_2$	Phen (2)	DMF	90	6	**2a** (0)	**4a** (87)
9	$Cu(acac)_2$ (2)	Phen (2)	DMAc[b]	90	6	**2a** (82)	
10	$Cu(acac)_2$ (2)	Phen (2)	1,4-dioxane	90	6	**2a** (83)	
11	$Cu(acac)_2$ (2)	Phen (2)	toluene	90	6	**2a** (86)	
12	**$Cu(acac)_2$ (2)**	**Phen (2)**	**EtCN**	90	6	**2a (90)**	
13	$Cu(acac)_2$ (0.5)	Phen (0.5)	EtCN	90	8	**2a** (68)[c]	**3a** (16)[c]
14	$Cu(acac)_2$ (2)	2,2′-bipyridine (2)	EtCN	90	6	**2a** (76)	
15	$Cu(acac)_2$ (2)	pyridine (2)	EtCN	90	6	**2a** (0)	**1a** (97)[d]
16	$Cu(acac)_2$ (2)	–	EtCN	90	6	**2a** (0)	**1a** (85)[d]
17	$Cu(acac)_2$ (2)	Phen (2)	EtCN	80	6	**2a** (86)	
18	$Cu(acac)_2$ (2)	Phen (2)	EtCN	70	6	**2a** (71)	
19[e]	$Cu(acac)_2$ (2)	Phen (2)	EtCN	90	6	**2a** (83)	

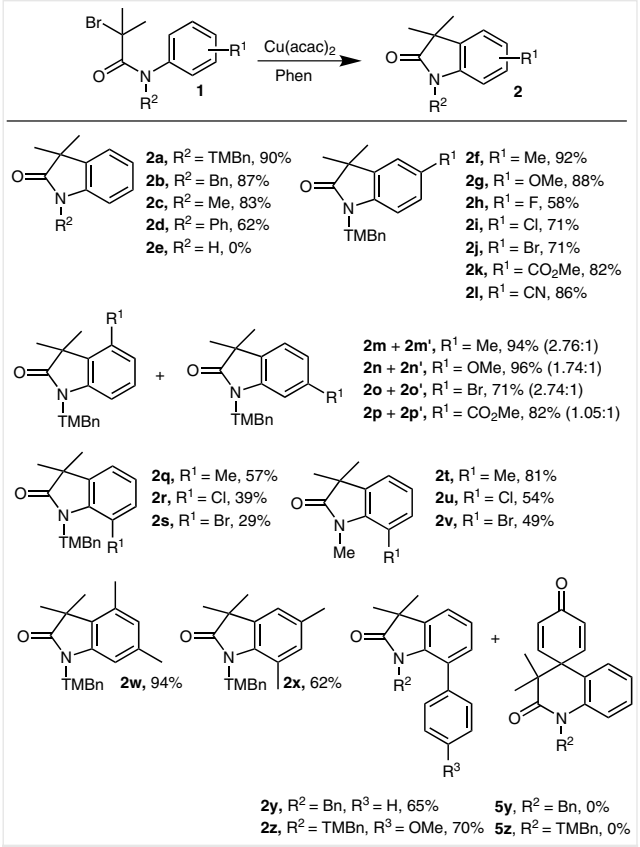
[a] Isolated yield.
[b] DMAc: *N*,*N*-Dimethylacetamide.
[c] Based on 76% conversion.
[d] The starting **1a** was recovered.
[e] Under air.



Scheme 2 Proposed reaction mechanism for the formation of 3,3′-disubstituted oxindoles

yield (entry 19). With these screening studies, the optimal conditions were established using $Cu(acac)_2$ (2 equiv) and Phen (2 equiv) in EtCN under N_2 atmosphere (entry 12).

Under the optimal $Cu(acac)_2$/Phen conditions (Table 1, entry 12), the scope and limitations of this copper-promoted cyclization reaction were then investigated and the results are summarized in Scheme 3. *N*-Alkyl protecting acylamides **1a–c** underwent efficient intramolecular ring closure. With **1a** bearing a bulkier TMBn group, the reaction provided the expected oxindole **2a** in best yield (90%), presumably because the introduction of a larger N-protecting group would shift the equilibrium in favor of the *anti*-I conformer, which could cyclize to produce **2a** (Scheme 2). *N*-Phenylacylamide **1d** is also suitable for this transformation and the corresponding oxindole **2d** was formed in moderate yield (62%). Acylamide **1e** bearing a free NH group failed to give the desired product **2e** due to the dominance of the *syn*-conformer with unfavorable geometry for cyclization. Next, we turned our attention to the substituent effect on the *N*-aryl ring of acylamides **1**. A variety of electron-donating groups such as methyl and methoxy as well as electron-withdrawing groups such as fluoro, chloro, bromo, methoxycarbonyl, and cyano at the *para*-position of the aniline moiety were well tolerated. The electron-donating substituents clearly gave higher yields than their electron-withdrawing counterparts (**2f–l**). Halo-substituted oxindoles **2h–j**, which could allow for further modifications, were synthesized in lower yields. As for the *meta*-substituted substrates **1m–p**, the reaction provided a mixture of two regioisomers in good yields; however, the regioselectivity is rather poor. In most cases, products **2m–p** derived from cyclization at the more hindered site are preferred.[22] Furthermore, the *ortho*-substituents exhibit a particularly distinct steric hindrance effect, and the corresponding oxindoles **2q–s** and **2x** were obtained in relatively low yields. This is presumably due to the steric effect between the *ortho*-substituent and *N*-TMBn group. Indeed, as the size of R^2 group decreased, the reaction yields of **2t–v** (R^2 = Me) were increased. In spite of the size of the phenyl group, substrates **1y** and **1z** bearing a phenyl group at *ortho*-position displayed high reactivity in this transformation and provided the corresponding oxindoles in moderate yields (**2y** and **2z**). The other expected spirodihydroquinolinones **5y** and **5z**, generated via the 6-*exo*-trig (6-*ipso*) cyclization, were not found.[18b,23] This $Cu(acac)_2$-promoted carbocyclization of α-bromo-*N*-arylacylamides **1** provides an efficient method for the synthesis of 3,3′-disubstituted oxindoles **2** using easily available Phen as the ligand.[24]

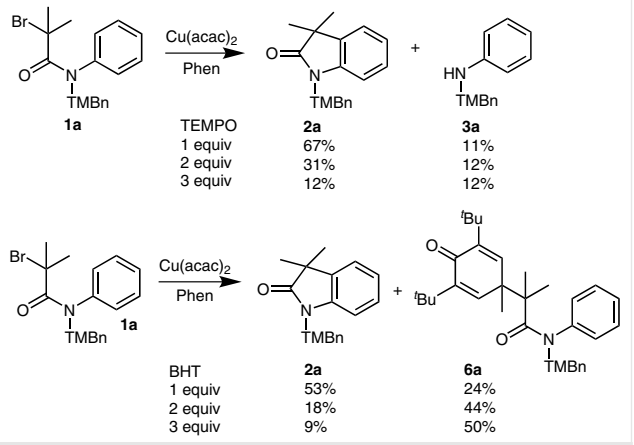


Scheme 3 $Cu(acac)_2$-promoted carbocyclization reactions of α-bromo-*N*-arylacylamides **1**. *Reaction conditions*: The reaction was carried out using **1** (0.40 mmol) with $Cu(acac)_2$ (2 equiv) and Phen (2 equiv) in EtCN (3 mL) at 90 °C for 6 h under N_2 atmosphere. Isolated yields are shown. The product ratios were determined by ^{1}H NMR spectroscopy.

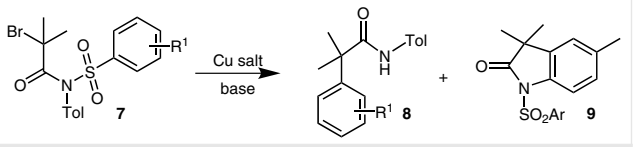
To gain a further understanding about the reaction mechanism, several inhibition experiments were conducted. As shown in Scheme 4, the reaction of **1a** with $Cu(acac)_2$ and Phen proceeded under the optimized conditions in the presence of a radical scavenger TEMPO (2,2,6,6-tetramethylpiperidinyloxy, 1 equiv) and a 67% yield of **2a** was obtained. By increasing the loading of TEMPO to 3 equivalents, the yield of the target product **2a** was further reduced to 12%. Another radical inhibitor BHT (2,6-di-*tert*-butyl-4-

methylphenol, 3 equiv) was also applied. The reaction was suppressed and **2a** was isolated in low yield (9%). In addition, the radical-trapping adduct **6a** was also formed in 50% yield. These results could indicate that a radical intermediate is involved in the reaction.

On the basis of these observations and the previous literature reports,[8,10] we propose a plausible reaction mechanism for the generation of oxindoles **2** (see Scheme 2). The reaction of α-bromoacylamide **1a** with copper(II) species leads to the formation of carbamoylmethyl radical **I** and copper(III)[25] species via a single-electron transfer process. A five-membered-ring cyclization of radical **I** onto the aryl ring would generate the radical intermediate **II**. Subsequently, the copper(III) oxidation of **II** affords the corresponding carbocation **III**, followed by the loss of H^+, thus producing oxindole **2a** and regenerating the copper(II) species.

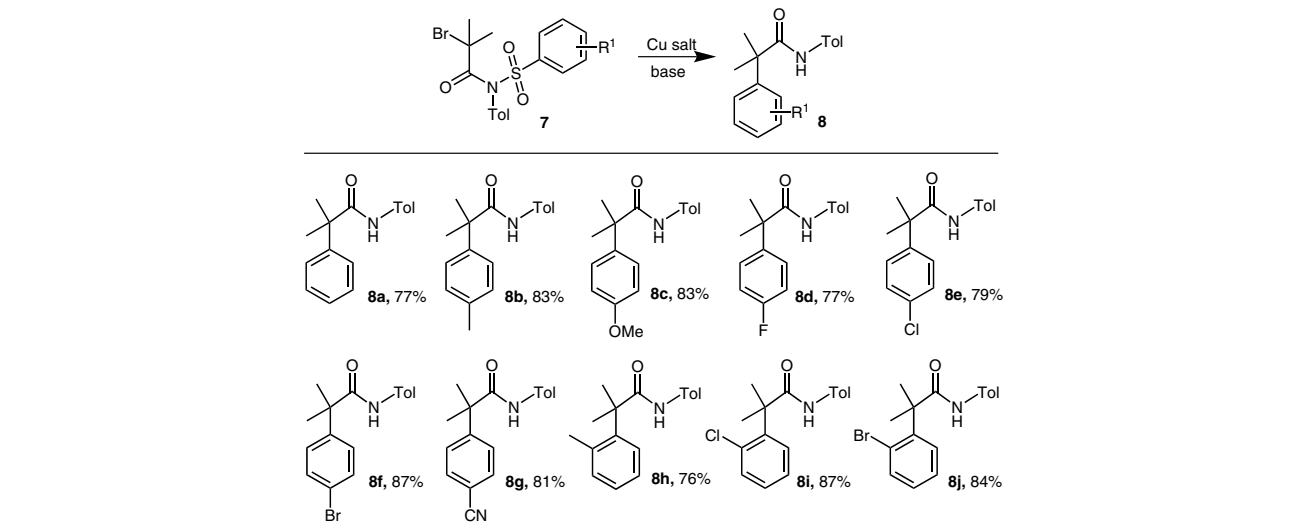


Scheme 4 Cyclization reactions of **1a** in the presence of radical scavengers



Scheme 5 Cyclization of *N*-arylsulfonyl-substituted acylamides

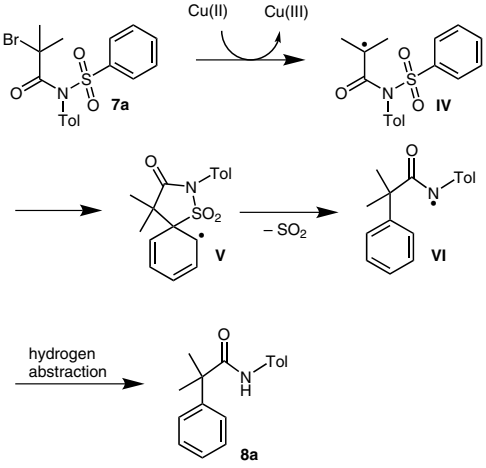
To further expand the substrate scope of this chemistry, we also extended the substrates to *N*-arylsulfonyl-substituted acylamides **7** (Scheme 5). Initially, we examined the reaction of **7a** (R^1 = H) with $Cu(acac)_2$ and Phen in EtCN at 90 °C. The α-phenylacylamide **8a** bearing a quaternary stereocenter, derived from the radical 1,4-aryl migration (via 5-*ipso* cyclization/desulfonylation) was produced exclusively in 77% yield (Scheme 6) and another expected oxindole **9a**, generated via the five-membered-ring radical cyclization, was not observed. Notably, the reaction proceeded with high site-selectivity through the carbon that was bonded to the SO_2 group in the starting acylamide **7a**. The scope and limitations of this transformation were next explored and the results are presented in Scheme 6. As expected, α-phenylacylamides **8** were formed successfully from the corresponding acylamides **7**. Both electron-donating (methyl and methoxy) and electron-withdrawing groups (fluoro, chloro, bromo, and cyano) at the *para*-position of the arylsulfonyl ring do not influence the reactivity remarkably and the target products **8a–g** could be obtained in good to excellent yields. In contrast to the results shown in Scheme 3, the *ortho*-substituents showed no significant steric effect on this reaction and the target products **8h–j** were generated in good yields. This $Cu(acac)_2$/Phen-promoted carbocyclization of *N*-arylsulfonyl-substituted acyl-



Scheme 6 $Cu(acac)_2$-promoted reactions of α-bromo-*N*-arylsulfonylacylamides **7**. *Reagents and conditions*: The reaction was carried out using **7** (0.45 mmol) with $Cu(acac)_2$ (2 equiv) and Phen (2 equiv) in EtCN (3 mL) at 90 °C for 6 h under N_2 atmosphere. Isolated yields are shown.

amides **7** provides a mild and facile route for the synthesis of α-arylacylamides **8** containing an all-carbon quaternary center.

α-Arylacylamides **8** are presumably formed by the reaction mechanism shown in Scheme 7.[26] Carbamoylmethyl radical **IV**, generated via a SET process of **7a**, undergoes a 5-*exo*-trig (5-*ipso*) radical cyclization onto the arylsulfonyl ring to generate radical **V**. Subsequently, the desulfonylation of radical **V**, followed by the extrusion of SO_2, takes place to produce amidyl radical **VI**. Finally, amidyl radical **VI** gets transformed into α-arylacylamide **8a** after hydrogen abstraction.



Scheme 7 Proposed reaction mechanism for the formation of α-arylacylamides

In conclusion, an efficient method has been developed for the synthesis of oxindoles and α-arylacylamides bearing an all carbon quaternary stereocenter from the readily prepared α-bromo-*N*-arylacylamides. Carbamoylmethyl radical, produced from the $Cu(acac)_2$-promoted SET reaction of α-bromo-*N*-arylacylamides, undergoes either a five-membered-ring cyclization onto the *N*-aryl ring to produce oxindoles or a 5-exo-*trig* (5-*ipso*) cyclization with the arylsulfonyl ring followed by desulfonylation to generate α-arylacylamides. In this $Cu(acac)_2$/Phen-promoted radical cyclization reaction, oxindoles and α-arylacylamides were formed in high chemoselectivity depending on the substituents on the nitrogen atom. This process has the advantages such as mild reaction conditions, high reaction yields and tolerance of a broad range of functional groups including methoxy, fluoro, chloro, bromo, methoxycarbonyl, and cyano groups.

Melting points are uncorrected. IR spectra were recorded on a Hitachi 260-30 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer. Chemical shifts are reported in ppm relative to TMS as internal reference. The multiplicity of the ^{13}C NMR signals was determined by means of DEPT 135 experiments. Elemental analyses were performed with Heraeus CHN-Rapid Analyzer. Mass spectra were recorded on a Jeol JMS-SX 102A mass spectrometer. Analytical TLC was performed with precoated silica gel 60 F_{254} plates (0.25 mm thick) from EM Laboratories and visualized by UV. The reaction mixture was purified by column chromatography over EM Laboratories silica gel (70–230 mesh).

The preparation of α-bromo-*N*-arylacylamides **1** and α-bromo-*N*-arylsulfonylacylamides **7** are provided in the Supporting Information.

$Cu(acac)_2$-Promoted Carbocyclization Reactions of α-Bromo-*N*-arylacylamides 1; 3,3-Dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2a); Typical Procedure

A mixture of α-bromo-*N*-arylacylamide **1a** (150 mg, 0.40 mmol), $Cu(acac)_2$ (212 mg, 0.81 mmol) and Phen (147 mg, 0.81 mmol) in EtCN (3 mL) was stirred at 90 °C for 6 h under N_2 atmosphere. The reaction mixture was then diluted with EtOAc (50 mL), washed with H_2O (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography over silica gel (20 g) (eluent: 1:20 EtOAc–hexane) followed by crystallization (EtOAc–hexane) to give **2a** as colorless needles; yield: 106 mg (90%); mp 93–94 °C (EtOAc–hexane).

IR (KBr): 2975, 1710, 1610, 1485, 1350 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.31 (s, 6 H, 2 × CH_3), 4.98 (s, 2 H, NCH_2), 6.38 (dd, *J* = 7.5, 1.2 Hz, 1 H, ArH), 6.85 (s, 2 H, ArH), 6.95 (td, *J* = 7.5, 1.2 Hz, 1 H, ArH), 7.00 (td, *J* = 7.5, 1.5 Hz, 1 H, ArH), 7.16 (dd, *J* = 7.5, 1.5 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.8 (q), 24.6 (2 q), 39.5 (t), 43.8 (s), 109.4 (d), 122.1 (2 d), 127.5 (d), 128.4 (s), 129.7 (2 d), 135.9 (s), 137.14 (2 s), 137.19 (s), 141.9 (s), 180.9 (s).

Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77. Found: C, 81.89; H, 7.92; N, 4.75.

1-Benzyl-3,3-dimethylindolin-2-one (2b)

Yield: 101mg (87%); colorless crystals; mp 90–91 °C (EtOAc–hexane).

IR (KBr): 1715, 1615, 1490, 1380, 1360 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 6 H, 2 × CH_3), 4.92 (s, 2 H, NCH_2), 6.72 (d, *J* = 7.6 Hz, 1 H, ArH), 7.02 (t, *J* = 7.6 Hz, 1 H, ArH), 7.13 (td, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.21 (d, *J* = 7.6 Hz, 1 H, ArH), 7.25–7.34 (m, 5 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.5 (2 q), 43.5 (t), 44.2 (s), 109.0 (d), 122.3 (d), 122.5 (d), 127.1 (2 d), 127.49 (d), 127.53 (d), 128.7 (2 d), 135.8 (s), 136.1 (s), 141.6 (s), 181.4 (s).

Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.32; H, 6.83; N, 5.53.

1,3,3-Trimethylindolin-2-one (2c)

Yield: 85 mg (83%); yellow liquid.

IR (neat): 1715, 1615, 1470, 1350, 1125 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.37 (s, 6 H, 2 × CH_3), 3.21 (s, 3 H, CH_3), 6.84 (d, *J* = 7.6 Hz, 1 H, ArH), 7.06 (t, *J* = 7.6 Hz, 1 H, ArH), 7.20 (d, *J* = 7.6 Hz, 1 H, ArH), 7.25 (t, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.2 (2 q), 26.0 (q), 44.0 (s), 107.9 (d), 122.1 (d), 122.3 (d), 127.5 (d), 135.7 (s), 142.5 (s), 181.2 (s)

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{11}H_{13}NO$: 175.0997; found: 175.0991.

3,3-Dimethyl-1-phenylindolin-2-one (2d)

Yield: 70 mg (62%); colorless crystals; mp 84–85 °C (EtOAc–hexane).

IR (KBr): 1725, 1610, 1590, 1480, 1205 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.49 (s, 6 H, 2 × CH_3), 6.85 (d, *J* = 7.4 Hz, 1 H, ArH), 7.10 (t, *J* = 7.4 Hz, 1 H, ArH), 7.19 (t, *J* = 7.4 Hz, 1 H, ArH), 7.27 (t, *J* = 7.4 Hz, 1 H, ArH), 7.39 (d, *J* = 7.4 Hz, 1 H, ArH), 7.42 (d, *J* = 7.7 Hz, 2 H, ArH), 7.52 (d, *J* = 7.7 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.7 (2 q), 44.3 (s), 109.3 (d), 122.6 (d), 122.9 (d), 126.5 (2 d), 127.5 (d), 127.8 (d), 129.5 (2 d), 134.6 (s), 135.6 (s), 142.5 (s), 180.7 (s).

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.71; H, 6.38; N, 5.83.

3,3,5-Trimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2f)

Yield: 110 mg (92%); colorless crystals; mp 137–138 °C (EtOAc–hexane).

IR (KBr): 1715, 1495, 1330 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 6 H, 2 × CH_3), 2.25 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 2.30 (s, 6 H, 2 × CH_3), 4.96 (s, 2 H, NCH_2), 6.26 (d, *J* = 8.0 Hz, 2 H, ArH), 6.79 (d, *J* = 8.0 Hz, 2 H, ArH), 6.84 (s, 2 H, ArH), 6.98 (s, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.8 (q), 20.9 (q), 24.7 (2 q), 39.5 (t), 43.8 (s), 109.1 (d), 122.9 (d), 127.8 (d), 128.5 (s), 129.6 (2 d), 131.5 (s), 136.0 (s), 137.1 (3 s), 139.4 (s), 180.8 (s).

Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 81.96; H, 8.22; N, 4.52.

5-Methoxy-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2g)

Yield: 105 mg (88%); colorless crystals; mp 131–132 °C (EtOAc–hexane).

IR (KBr): 1700, 1600, 1490, 1430 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.30 (s, 6 H, 2 × CH_3), 3.72 (s, 3 H, OCH_3), 4.95 (s, 2 H, NCH_2), 6.25 (d, *J* = 8.6 Hz, 1 H, ArH), 6.52 (dd, *J* = 8.6, 2.6 Hz, 1 H, ArH), 6.77 (d, *J* = 2.6 Hz, 1 H, ArH), 6.84 (s, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.7 (2 q), 39.5 (t), 44.2 (s), 55.6 (q), 109.7 (d), 109.8 (d), 111.4 (d), 128.5 (s), 129.7 (2 d), 135.3 (s), 137.2 (3 s), 137.4 (s), 155.6 (s), 180.6 (s).

Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 78.00; H, 7.85; N, 4.32.

5-Fluoro-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2h)

Yield: 69 mg (58%); colorless crystals; mp 128–129 °C (EtOAc–hexane).

IR (KBr): 1710, 1610, 1490, 1445 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.29 (s, 6 H, 2 × CH_3), 4.96 (s, 2 H, NCH_2), 6.26 (dd, *J* = 8.6, 4.3 Hz, 1 H, ArH), 6.69 (td, *J* = 8.6, 2.6 Hz, 1 H, ArH), 6.85 (s, 2 H, ArH), 6.90 (dd, *J* = 8.6, 2.6 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.5 (2 q), 39.6 (t), 44.2 (s), 109.9 (dd, *J* = 8.0 Hz), 110.2 (d, *J* = 24.1 Hz), 113.7 (dd, *J* = 23.1 Hz), 128.1 (s), 129.7 (2 d), 137.1 (2 d), 137.4 (s), 137.6 (sd, *J* = 6.0 Hz), 137.7 (s), 159.0 (sd, *J* = 241.4 Hz), 180.5 (s).

Anal. Calcd for $C_{20}H_{22}FNO$: C, 77.14; H, 7.12; N, 4.50. Found: C, 77.26; H, 7.20; N, 4.46.

5-Chloro-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2i)

Yield: 84 mg (71%); colorless crystals; mp 145–146 °C (EtOAc–hexane).

IR (KBr): 1715, 1610, 1485, 1325 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.28 (s, 6 H, 2 × CH_3), 4.96 (s, 2 H, NCH_2), 6.25 (d, *J* = 8.4 Hz, 1 H, ArH), 6.85 (s, 2 H, ArH), 6.96 (dd, *J* = 8.4, 2.1 Hz, 1 H, ArH), 7.13 (d, *J* = 2.1 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.5 (2 q), 39.6 (t), 44.0 (s), 110.4 (d), 122.7 (d), 127.5 (d), 127.6 (s), 128.0 (s), 129.8 (2 d), 137.1 (2 s), 137.5 (s), 137.6 (s), 140.4 (s), 180.4 (s).

Anal. Calcd for $C_{20}H_{22}ClNO$: C, 73.27; H, 6.76; N, 4.27. Found: C, 73.21; H, 6.75; N, 4.25.

5-Bromo-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2j)

Yield: 88 mg (71%); colorless crystals; mp 166–167 °C (EtOAc–hexane).

IR (KBr): 1715, 1605, 1485, 1465 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 6 H, 2 × CH_3), 2.25 (s, 3 H, CH_3), 2.27 (s, 6 H, 2 × CH_3), 4.92 (s, 2 H, NCH_2), 6.25 (d, *J* = 8.4 Hz, 1 H, ArH), 6.86 (s, 2 H, ArH), 7.12 (dd, *J* = 8.4, 2.1 Hz, 1 H, ArH), 7.29 (d, *J* = 2.1 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.6 (2 q), 39.6 (t), 44.0 (s), 110.9 (d), 115.0 (s), 125.5 (d), 127.9 (s), 129.8 (2 d), 130.4 (d), 137.1 (2 s), 137.5 (s), 138.0 (s), 140.9 (s), 180.3 (s).

Anal. Calcd for $C_{20}H_{22}BrNO$: C, 64.52; H, 5.96; N, 3.76. Found: C, 64.54; H, 5.95; N, 3.71.

5-(Methoxycarbonyl)-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2k)

Yield: 99 mg (82%); colorless needles; mp 169–170 °C (EtOAc–hexane).

IR (KBr): 1715, 1620, 1295, 1250 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.29 (s, 6 H, 2 × CH_3), 3.86 (s, 3 H, OCH_3), 5.00 (s, 2 H, NCH_2), 6.39 (d, *J* = 8.3 Hz, 1 H, ArH), 6.86 (s, 2 H, ArH), 7.75 (dd, *J* = 8.3, 1.7 Hz, 1 H, ArH), 7.83 (d, *J* = 1.7 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.5 (2 q), 39.7 (t), 43.6 (s), 51.9 (q), 108.9 (d), 123.4 (d), 124.0 (s), 127.9 (s), 129.8 (2 d), 130.3 (d), 135.8 (s), 137.1 (2 s), 137.5 (s), 146.1 (s), 166.9 (s), 181.2 (s).

Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.19; N, 3.99. Found: C, 75.04; H, 7.17; N, 3.95.

5-Cyano-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2l)

Yield: 115 mg (86%); colorless crystals; 208–209 °C (EtOAc–hexane).

IR (KBr): 2220, 1720, 1615, 1490, 1330 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 6 H, 2 × CH_3), 2.27 (s, 3 H, CH_3), 2.28 (s, 6 H, 2 × CH_3), 4.99 (s, 2 H, NCH_2), 6.39 (d, *J* = 8.3 Hz, 1 H, ArH), 6.87 (s, 2 H, ArH), 7.31 (dd, *J* = 8.3, 1.7 Hz, 1 H, ArH), 7.40 (d, *J* = 1.7 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.2 (2 q), 20.8 (q), 24.4 (2 q), 39.7 (t), 43.6 (s), 105.2 (s), 109.7 (d), 119.2 (s), 125.5 (d), 127.4 (s), 129.9 (2 d), 132.9 (d), 136.7 (s), 137.0 (2 d), 137.8 (s), 145.8 (s), 180.5 (s).

Anal. Calcd for $C_{21}H_{22}N_2O$: C, 79.21; H, 6.96; N, 8.80. Found: C, 79.31; H, 6.98; N, 8.83.

3,3,4-Trimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2m) and 3,3,6-Trimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2m′)

Yield: 112 mg (94%, 2.76:1).

2m

Colorless crystals; mp 157–158 °C (EtOAc–hexane).

IR (KBr): 2970, 2925, 1705, 1595, 1470 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (s, 6 H, 2 × CH_3), 2.25 (s, 3 H, CH_3), 2.30 (s, 6 H, 2 × CH_3), 2.37 (s, 3 H, CH_3), 4.97 (s, 2 H, NCH_2), 6.27 (d, *J* = 7.8 Hz, 1 H, ArH), 6.72 (d, *J* = 7.8 Hz, 1 H, ArH), 6.83 (s, 2 H, ArH), 6.91 (t, *J* = 7.8 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.2 (q), 20.3 (2 q), 20.8 (q), 22.6 (2 q), 39.6 (t), 44.6 (s), 107.2 (d), 124.7 (d), 127.3 (d), 128.6 (s), 129.7 (2 d), 132.6 (s), 133.8 (s), 137.1 (3 s), 142.2 (s), 180.9 (s).

Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 82.12; H, 8.21; N, 4.52.

4-Methoxy-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2n) and 6-Methoxy-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2n′)

Yield: 195 mg (96%, 1.74:1).

2n

Colorless crystals; mp 162–163 °C (EtOAc–hexane).

IR (KBr): 1715, 1600, 1470, 1260 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 6 H, 2 × CH_3), 2.25 (s, 3 H, CH_3), 2.30 (s, 6 H, 2 × CH_3), 3.81 (s, 3 H, OCH_3), 4.95 (s, 2 H, NCH_2), 6.05 (d, *J* = 8.2 Hz, 1 H, ArH), 6.51 (d, *J* = 8.2 Hz, 1 H, ArH), 6.83 (s, 2 H, ArH), 6.96 (t, *J* = 8.2 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.8 (q), 22.3 (2 q), 39.6 (t), 44.2 (s), 55.2 (q), 102.8 (d), 105.4 (d), 121.2 (s), 128.6 (d), 128.7 (s), 129.6 (2 d), 137.07 (s), 137.11 (2 s), 143.1 (s), 155.9 (s), 181.3 (s).

Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.95; H, 7.83; N, 4.27.

2n′

Colorless crystals; mp 138–139 °C (EtOAc–hexane).

IR (KBr): 1715, 1625, 1500, 1165 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 6 H, 2 × CH_3), 2.25 (s, 3 H, CH_3), 2.31 (s, 6 H, 2 × CH_3), 3.59 (s, 3 H, OCH_3), 4.96 (s, 2 H, NCH_2), 6.00 (d, *J* = 2.2 Hz, 1 H, ArH), 6.46 (dd, *J* = 8.1, 2.2 Hz, 1 H, ArH), 6.85 (s, 2 H, ArH), 7.04 (d, *J* = 8.1 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.8 (q), 24.9 (2 q), 39.5 (t), 43.3 (s), 55.1 (q), 97.0 (d), 106.5 (d), 122.5 (d), 127.8 (s), 128.4 (s), 129.7 (2 d), 137.2 (2 s), 137.3 (s), 143.0 (s), 159.4 (s), 181.5 (s).

Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.97; H, 7.77; N, 4.27.

4-Bromo-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2o) and 6-Bromo-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2o′)

Yield: 147 mg (71%, 2.74:1).

2o

Colorless crystals; mp 137–138 °C (EtOAc–hexane).

IR (KBr): 1715, 1600, 1450, 1325, 1170 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.29 (s, 6 H, 2 × CH_3), 4.97 (s, 2 H, NCH_2), 6.34 (d, *J* = 8.0 Hz, 1 H, ArH), 6.85 (s, 2 H, ArH), 6.86 (t, *J* = 8.0 Hz, 1 H, ArH), 7.06 (d, *J* = 8.0 Hz,1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 21.6 (2 q), 39.6 (t), 46.1 (s), 108.4 (d), 118.5 (s), 126.4 (d), 128.1 (s), 129.0 (d), 129.8 (2 d), 133.2 (s), 137.1 (2 s), 137.4 (s), 144.0 (s), 180.3 (s).

Anal. Calcd for $C_{20}H_{22}BrNO$: C, 64.52; H, 5.96; N, 3.76. Found: C, 64.45; H, 5.99; N, 3.70.

2o′

Colorless crystals; mp 125–126 °C (EtOAc–hexane).

IR (KBr): 1715, 1600, 1485, 1330, 1170 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (s, 6 H, 2 × CH_3), 2.27 (s, 3 H, CH_3), 2.30 (s, 6 H, 2 × CH_3), 4.94 (s, 2 H, NCH_2), 6.53 (d, *J* = 1.7 Hz, 1 H, ArH), 6.87 (s, 2 H, ArH), 7.01 (d, *J* = 7.9 Hz, 1 H, ArH), 7.09 (dd, *J* = 7.9, 1.7 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.5 (2 q), 39.6 (t), 43.6 (s), 112.9 (d), 120.9 (s), 123.4 (d), 124.9 (d), 127.7 (s), 129.8 (2 d), 134.8 (s), 137.1 (2 s), 137.6 (s), 143.3 (s), 180.7 (s).

Anal. Calcd for $C_{20}H_{22}BrNO$: C, 64.52; H, 5.96; N, 3.76. Found: C, 64.49; H, 6.08; N, 3.67.

4-(Methoxycarbonyl)-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2p) and 6-(Methoxycarbonyl)-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2p′)

Yield: 167 mg (82%, 1.05:1).

2p

Colorless crystals; mp 148–149 °C (EtOAc–hexane).

IR (KBr): 1730, 1715, 1600, 1455 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.30 (s, 6 H, 2 × CH_3), 3.91 (s, 3 H, OCH_3), 5.01 (s, 2 H, NCH_2), 6.59 (dd, *J* = 8.0, 0.8 Hz, 1 H, ArH), 6.85 (s, 2 H, ArH), 7.08 (t, *J* = 8.0 Hz, 1 H, ArH), 7.55 (dd, *J* = 8.0, 0.8 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.8 (q), 22.4 (2 q), 39.7 (t), 45.9 (s), 52.0 (q), 113.1 (d), 124.2 (d), 127.1 (s), 127.5 (d), 128.1 (s), 129.8 (2 d), 136.5 (s), 137.0 (2 s), 137.3 (s), 143.3 (s), 166.4 (s), 181.2 (s).

Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.21; H, 7.19; N, 3.94.

2p′

Colorless crystals; mp 131–132 °C (EtOAc–hexane).

IR (KBr): 1720, 1465, 1450, 1280 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (s, 6 H, 2 × CH_3), 2.26 (s, 3 H, CH_3), 2.35 (s, 6 H, 2 × CH_3), 3.83 (s, 3 H, OCH_3), 4.99 (s, 2 H, NCH_2), 6.88 (s, 2 H, ArH), 7.15 (s, 1 H, ArH), 7.21 (d, *J* = 7.8 Hz, 1 H, ArH), 7.68 (dd, *J* = 7.8, 1.4 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.9 (q), 24.4 (2 q), 39.6 (t), 44.1 (s), 52.1 (q), 110.3 (d), 121.9 (d), 124.0 (d), 127.9 (s), 129.7 (2 d), 137.3 (3 s), 137.5 (s), 141.0 (s), 142.2 (s), 166.7 (s), 180.5 (s).

Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.23; H, 7.19; N, 3.95.

3,3,7-Trimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2q)

Yield: 68 mg (57%); colorless crystals; mp 122–123 °C (EtOAc–hexane).

IR (KBr): 1705, 1605, 1460, 1355, 1175 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 6 H, 2 × CH_3), 2.21 (s, 9 H, 3 × CH_3), 2.24 (s, 3 H, CH_3), 5.16 (s, 2 H, NCH_2), 6.79 (s, 2 H, NCH_2), 6.90–6.97 (m, 2 H, ArH), 7.03–7.08 (m, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.6 (q), 20.5 (2 q), 20.7 (q), 24.7 (2 q), 42.7 (t), 43.2 (s), 120.0 (s), 120.3 (d), 122.4 (d), 130.1 (2 d), 131.4 (s), 131.6 (d), 135.7 (2 s), 136.2 (s), 136.7 (s), 140.8 (s), 182.3 (s).

Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 82.08; H, 8.21; N, 4.52.

7-Chloro-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2r)

Yield: 47 mg (39%); colorless crystals; mp 139–140 °C (EtOAc–hexane).

IR (KBr): 1710, 1460, 1380, 1345, 1165 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 6 H, 2 × CH_3), 2.23 (s, 3 H, CH_3), 2.27 (s, 6 H, 2 × CH_3), 5.36 (s, 2 H, NCH_2), 6.79 (s, 2 H, ArH), 6.96 (t, *J* = 7.7 Hz, 1 H, ArH), 7.10 (dd, *J* = 7.7, 1.1 Hz, 1 H, ArH), 7.16 (dd, *J* = 7.7, 1.1 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.5 (2 q), 20.8 (q), 24.6 (2 q), 42.3 (t), 43.5 (s), 115.3 (s), 121.0 (d), 123.2 (d), 129.6 (2 d), 130.4 (d), 130.8 (s), 136.23 (s), 136.30 (2 s), 138.77 (s), 138.82 (s), 181.6 (s).

Anal. Calcd for $C_{20}H_{22}ClNO$: C, 73.27; H, 6.76; N, 4.27. Found: C, 73.17; H, 6.75; N, 4.22.

7-Bromo-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2s)

Yield: 36 mg (29%); colorless crystals; mp 165–166 °C (EtOAc–hexane).

IR (KBr): 1710, 1460, 1445, 1345, 1165 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 6 H, 2 × CH_3), 2.23 (s, 3 H, CH_3), 2.27 (s, 6 H, 2 × CH_3), 5.39 (s, 2 H, NCH_2), 6.79 (s, 2 H, ArH), 6.90 (t, *J* = 7.6 Hz, 1 H, ArH), 7.14 (d, *J* = 7.6 Hz, 1 H, ArH), 7.37 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.5 (2 q), 20.8 (q), 24.5 (2 q), 42.4 (t), 43.4 (s), 102.3 (s), 121.6 (d), 123.5 (d), 129.6 (2 d), 130.6 (s), 133.8 (d), 136.21 (s), 136.25 (2 s), 139.1 (s), 140.2 (s), 181.8 (s).

Anal. Calcd for $C_{20}H_{22}BrNO$: C, 64.52; H, 5.96; N, 3.79. Found: C, 64.63; H, 6.02; N, 3.72.

1,3,3,7-Tetramethylindolin-2-one (2t)

Yield: 85 mg (81%); colorless oil.

IR (neat): 1705, 1600, 1465, 1345, 1080 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 6 H, 2 × CH_3), 2.59 (s, 3 H, CH_3), 3.50 (s, 3 H, NCH_3), 6.91–7.00 (m, 2 H, ArH), 7.04 (d, *J* = 7.0 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.0 (q), 24.7 (2 q), 29.5 (q), 43.5 (s), 119.6 (s), 120.2 (d), 122.4 (d), 131.3 (d), 136.5 (s), 140.3 (s), 182.1 (s)

HRMS(EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{15}NO$: 189.1154; found: 189.1157.

7-Chloro-1,3,3-trimethylindolin-2-one (2u)

Yield: 79 mg (54%); colorless oil.

IR (neat): 1715, 1455, 1365, 1085, 1065 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 6 H, 2 × CH_3), 3.59 (s, 3 H, NCH_3), 6.96 (t, *J* = 7.7 Hz, 1 H, ArH), 7.08 (d, *J* = 7.7 Hz, 1 H, ArH), 7.18 (dd, *J* = 7.7, 0.7 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.6 (2 q), 29.5 (q), 43.9 (s), 115.4 (s), 120.8 (d) 123.3(d), 129.9 (d), 138.5 (s), 138.6 (s), 181.5 (s).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{11}H_{12}ClNO$: 209.0607; found: 209.0605.

7-Bromo-1,3,3-trimethylindolin-2-one (2v)

Yield: 75 mg (49%); colorless oil.

IR (neat): 1700, 1455, 1360, 1335, 1060 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 6 H, 2 × CH_3), 3.60 (s, 3 H, NCH_3), 6.90 (t, *J* = 7.7 Hz, 1 H, ArH), 7.12 (d, *J* = 7.7 Hz, 1 H, ArH), 7.36 (d, *J* = 7.7 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.6 (2 q), 29.7 (q), 43.9 (s), 102.3 (s), 121.3 (d), 123.6 (d), 133.2 (d), 138.9 (s), 139.9 (s), 181.6 (s).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{11}H_{12}BrNO$: 253.0102; found: 253.0095.

3,3,4,6-Tetramethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2w)

Yield: 115 mg (94%); colorless crystals; mp 142–143 °C (EtOAc–hexane).

IR (KBr): 1700, 1615, 1455, 1340, 1165 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 6 H, 2 × CH_3), 2.13 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.31 (s, 6 H, 2 × CH_3), 2.33 (s, 3 H, CH_3), 4.94 (s, 2 H, NCH_2), 6.13 (s, 1 H, ArH), 6.55 (s, 1 H, ArH), 6.84 (s, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.1 (q), 20.3 (2 q), 20.8 (q), 21.5 (q), 22.7 (2 q), 39.6 (t), 44.4 (s), 108.1 (d), 125.3 (d), 128.7 (s), 129.6 (2 d), 129.7 (s), 133.5 (s), 137.03 (s), 137.07 (2 s), 137.10 (s), 142.4 (s), 181.3 (s).

Anal. Calcd for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.15; H, 8.53; N, 4.31.

3,3,5,7-Tetramethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2x)

Yield: 100 mg (62%); colorless crystals; mp 157–158 °C (EtOAc–hexane).

IR (KBr): 1710, 1480, 1455, 1335, 1165 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 6 H, 2 × CH_3), 2.15 (s, 3 H, CH_3), 2.20 (s, 6 H, 2 × CH_3), 2.23 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 5.13 (s, 2 H, NCH_2), 6.72 (s, 1 H, ArH), 6.78 (s, 2 H, ArH), 6.87 (s, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.5 (q), 20.5 (2 q), 20.7 (2 q), 24.7 (2 q), 42.6 (t), 43.2 (s), 119.7 (s), 121.1 (d), 130.0 (2 d), 131.4 (s), 131.8 (s), 132.1 (d), 135.8 (2 s), 136.1 (s), 136.8 (s), 138.3 (s), 182.2 (s).

Anal. Calcd for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.00; H, 8.51; N, 4.35.

1-Benzyl-3,3-dimethyl-7-phenylindolin-2-one (2y)

Yield: 109 mg (65%); yellow oil.

IR (neat): 1710, 1600, 1440, 1345, 1160 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.51 (s, 6 H, 2 × CH_3), 4.68 (s, 2 H, NCH_2), 6.46 (d, *J* = 7.5 Hz, 2 H, ArH), 6.94 (dd, *J* = 7.5, 1.2 Hz, 1 H, ArH), 6.96–7.11 (m, 6 H, ArH), 7.18 (t, *J* = 7.5 Hz, 2 H, ArH), 7.24 (dd, *J* = 7.5, 1.2 Hz, 1 H, ArH), 7.28 (t, *J* = 7.5 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 25.1 (2 q), 43.4 (s), 44.6 (t), 121.4 (d), 121.9 (d), 125.8 (2 d), 125.9 (s), 126.6 (d), 127.2 (d), 127.5 (2 d), 128.0 (2 d), 129.8 (2 d), 131.1 (d), 136.4 (s), 136.9 (s), 138.1 (s), 138.8 (s), 182.6 (s).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{23}H_{21}NO$: 327.1623; found: 327.1629.

7-(4-Methoxyphenyl)-3,3-dimethyl-1-(2,4,6-trimethylbenzyl)indolin-2-one (2z)

Yield: 88 mg (70%); colorless crystals; mp 145–146 °C (EtOAc–hexane).

IR (KBr): 1715, 1515, 1445, 1245 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 6 H, 2 × CH_3), 2.07 (s, 6 H, 2 × CH_3), 2.17 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 4.39 (s, 2 H, NCH_2), 6.67 (s, 2 H, ArH), 6.85 (d, *J* = 8.6 Hz, 2 H, ArH), 7.04–7.08 (m, 2 H, ArH), 7.16–7.27 (m, 3 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (2 q), 20.7 (q), 24.6 (2 q), 43.2 (t), 43.6 (s), 55.2 (q), 113.6 (2 d), 121.4 (d), 121.7 (d), 125.2 (s), 129.0 (2 d), 130.3 (s), 130.5 (2 d), 131.4 (d), 131.5 (s), 136.1 (s), 136.7 (2 s), 136.9 (s), 140.1 (s), 159.0 (s), 182.1 (s).

Anal. Calcd for $C_{27}H_{29}NO_2$: C, 81.17; H, 7.32; N, 3.51. Found: C, 81.16; H, 7.34; N, 3.46.

Radical Inhibition Experiments; Typical Procedure

A mixture of α-bromo-*N*-arylacylamide **1a** (150 mg, 0.40 mmol), $Cu(acac)_2$ (213 mg, 0.81 mmol), Phen (147 mg, 0.81 mmol), and TEMPO (190 mg, 1.21 mmol) in EtCN (3 mL) was stirred at 90 °C for 6 h under N_2 atmosphere. After workup as described as above, the crude product was purified by column chromatography over silica gel (20 g) (eluent: 1:20 EtOAc–hexane) followed by crystallization (EtOAc–hexane) to give **2a** (19 mg, 12%) and **3a** (11 mg, 12%).

***N*-(2,4,6-Trimethylbenzyl)aniline (3a)**

Yield: 11 mg (12 %); colorless crystals; mp 63–64 °C (EtOAc-hexane).

IR (KBr): 1605, 1505, 1480, 1430, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 2.33 (s, 6 H, 2 × CH_3), 3.38 (br s, 1 H, NH), 4.16 (s, 2 H, NCH_2), 6.64 (d, *J* = 7.5 Hz, 2 H, ArH), 6.71 (t, *J* = 7.5 Hz, 1 H, ArH), 6.88 (s, 2 H, ArH), 7.20 (t, *J* = 7.5 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.4 (2 q), 20.9 (q), 42.3 (t), 112.4 (2 d), 117.2 (d), 129.0 (2 d), 129.2 (2 d), 132.1 (s), 137.2 (s), 137.4 (2 s), 148.6 (s).

Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 85.28; H, 8.57; N, 6.20.

Radical-Trapping Adduct 6a

Yield: 103 mg (50%); colorless crystals; mp 152–153 °C (EtOAc–hexane).

IR (KBr): 1620, 1470, 1355, 1240, 1165 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (s, 6 H, 2 × CH_3), 1.23 (s, 18 H, 6 × CH_3), 1.39 (s, 3 H, CH_3), 1.92 (s, 6 H, 2 × CH_3), 2.22 (s, 3 H, CH_3), 4.95 (s, 2 H, NCH_2), 6.70 (s, 2 H, ArH), 6.74 (s, 2 H, ArH), 6.75 (d, *J* = 7.5 Hz, 2 H, ArH), 7.13 (t, *J* = 7.5 Hz, 2 H, ArH), 7.22 (t, *J* = 7.5 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.5 (2 q), 20.9 (q), 23.0 (q), 25.6 (2 q), 29.5 (2 q), 34.9 (2 s), 45.1 (s), 49.1 (t), 53.0 (s), 127.9 (d), 128.2 (2 d), 128.8 (2 d), 130.0 (s), 130.4 (2 d), 137.1 (s), 138.5 (2 s), 141.9 (s), 145.1 (2 d), 146.3 (2 s), 175.7 (s), 186.9 (s).

Anal. Calcd for $C_{35}H_{47}NO_2$: C, 81.82; H, 9.22; N, 2.73. Found: C, 81.95; H, 9.26; N, 2.69.

$Cu(acac)_2$-Promoted Reactions of α-Bromo-*N*-arylsulfonylacylamides 7; 2-Methyl-2-phenyl-*N*-(*p*-tolyl)propanamide (8a); Typical Procedure

A mixture of α-bromo-*N*-arylsulfonylacylamide **7a** (180 mg, 0.45 mmol), $Cu(acac)_2$ (237 mg, 0.91 mmol), and Phen (164 mg, 0.91 mmol) in EtCN (3 mL) was stirred at 90 °C for 6 h under N_2 atmosphere. After workup as described as above, the crude product was purified by column chromatography over silica gel (20 g) (eluent: 1:20 EtOAc–hexane) followed by crystallization (EtOAc–hexane) to give **8a** as colorless needles; yield: 88 mg (77%); mp 105–106 °C (EtOAc–hexane).

IR (KBr): 3285, 1655, 1600, 1515, 1400, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 6 H, 2 × CH_3), 2.27 (s, 3 H, CH_3), 6.73 (br s, 1 H, NH), 7.06 (d, *J* = 8.4 Hz, 2 H, ArH), 7.23 (d, *J* = 8.4 Hz, 2 H, ArH), 7.31 (t, *J* = 7.3 Hz, 1 H, ArH), 7.40 (t, *J* = 7.3 Hz, 2 H, ArH), 7.44 (d, *J* = 7.3 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 27.0 (2 q), 48.0 (s), 119.7 (2 q), 126.5 (2 d), 127.3 (d), 129.0 (2 d), 129.3 (2 d), 133.7 (s), 135.4 (s), 144.7 (s), 175.5 (s).

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.49; H, 7.60; N, 5.51.

2-Methyl-*N*,2-di(*p*-tolyl)propanamide (8b)

Yield: 81 mg (83%); colorless needles; mp 117–118 °C (EtOAc–hexane).

IR (KBr): 3355, 1665, 1600, 1515, 1400, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 6 H, 2 × CH_3), 2.27 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 6.77 (br s, 1 H, NH), 7.05 (d, *J* = 8.2 Hz, 2 H, ArH), 7.20 (d, *J* = 8.2 Hz, 2 H, ArH), 7.23 (d, *J* = 8.2 Hz, 2 H, ArH), 7.32 (d, *J* = 8.2 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 20.9 (q), 27.1 (2 q), 47.6 (s), 119.6 (2 d), 126.4 (2 d), 129.3 (2 d), 129.6 (2 d), 133.6 (s), 135.4 (s), 137.0 (s), 141.6 (s), 175.7 (s).

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.85; H, 7.93; N, 5.23.

2-(4-Methoxyphenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8c)

Yield: 112 mg (83%); colorless crystals; mp 104–105 °C (EtOAc–hexane).

IR (KBr): 3380, 1650, 1600, 1515, 1405, 1255 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 6 H, 2 × CH_3), 2.27 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 6.79 (br s, 1 H, NH), 6.92 (d, *J* = 8.9 Hz, 2 H, ArH), 7.05 (d, *J* = 8.3 Hz, 2 H, ArH), 7.23 (d, *J* = 8.3 Hz, 2 H, ArH), 7.35 (d, *J* = 8.9 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 27.1 (2 q), 47.3 (s), 55.3 (q), 114.2 (2 d), 119.6 (2 d), 127.7 (2 d), 129.3 (2 d), 133.6 (s), 135.4 (s), 136.6 (s), 158.6 (s), 175.8 (s).

Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.26; H, 7.47; N, 4.94. Found: C, 76.43; H, 7.50; N, 4.95.

2-(4-Fluorophenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8d)

Yield: 101 (77%); colorless crystals; mp 108–109 °C (EtOAc–hexane).

IR (KBr): 3340, 1650, 1600, 1510, 1315, 1235 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 6 H, 2 × CH_3), 2.28 (s, 3 H, CH_3), 6.72 (br s, 1 H, NH), 7.07 (d, *J* = 8.5 Hz, 2 H, ArH), 7.07 (t, *J* = 8.7 Hz, 2 H, ArH), 7.24 (d, *J* = 8.5 Hz, 2 H, ArH), 7.38–7.44 (m, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 27.2 (2 q), 47.5 (s), 115.75 (2 dd, $J_{C,F}$ = 21.1 Hz), 119.7 (2 d), 128.1 (2 dd, $J_{C,F}$ = 8.0 Hz), 129.4 (2 d), 133.9 (s), 135.2 (s), 140.5 (sd, $J_{C,F}$ = 3.0 Hz), 161.9 (sd, $J_{C,F}$ = 246.5 Hz), 175.1 (s).

Anal. Calcd for $C_{17}H_{18}FNO$: C, 75.25; H, 6.69; N, 5.16. Found: C, 75.24; H, 6.73; N, 5.14.

2-(4-Chlorophenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8e)

Yield: 105 (79%); colorless needles; mp 114–115 °C (EtOAc–hexane).

IR (KBr): 3320, 1650, 1595, 1515, 1400, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 6 H, 2 × CH_3), 2.28 (s, 3 H, CH_3), 6.75 (br s, 1 H, NH), 7.07 (d, *J* = 8.3 Hz, 2 H, ArH), 7.24 (d, *J* = 8.3 Hz, 2 H, ArH), 7.33–7.39 (m, 4 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 27.0 (2 q), 47.6 (s), 119.8 (2 d), 127.8 (2 d), 129.0 (2 d), 129.3 (2 d), 133.2 (s), 133.9 (s), 135.2 (s), 143.3 (s), 174.7 (s).

Anal. Calcd for $C_{17}H_{18}ClNO$: C, 70.95; H, 6.30; N, 4.87. Found: C, 70.97; H, 6.29; N, 4.87.

2-(4-Bromophenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8f)

Yield: 122 mg (87%); colorless crystals; mp 118–119 °C (EtOAc–hexane).

IR (KBr): 3325, 1650, 1515, 1475, 1395, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 6 H, 2 × CH_3), 2.28 (s, 3 H, CH_3), 6.74 (br s, 1 H, NH), 7.07 (d, *J* = 8.4 Hz, 2 H, ArH), 7.24 (d, *J* = 8.4 Hz, 2 H, ArH), 7.30 (d, *J* = 8.6 Hz, 2 H, ArH), 7.51 (d, *J* = 8.6 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 27.0 (2 q), 47.7 (s), 119.8 (2 d), 121.3 (s), 128.2 (2 d), 129.4 (2 d), 132.0 (2 d), 134.0 (s), 135.2 (s), 143.8 (s), 174.7 (s).

Anal. Calcd for $C_{17}H_{18}BrNO$: C, 61.46; H, 5.46; N, 4.22. Found: C, 61.47; H, 5.51; N, 4.22.

2-(4-Cyanophenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8g)

Yield: 122 mg (81%); colorless crystals; mp 110–111 °C (EtOAc–hexane).

IR (KBr): 3325, 2230,1655, 1605, 1515, 1400, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 6 H, 2 × CH_3), 2.29 (s, 3 H, CH_3), 6.83 (br s, 1 H, NH), 7.08 (d, *J* = 8.4 Hz, 2 H, ArH), 7.27 (d, *J* = 8.4 Hz, 2 H, ArH), 7.54 (d, *J* = 8.4 Hz, 2 H, ArH), 7.65 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 26.8 (2 q), 48.2 (s), 111.1 (s), 118.5 (s), 120.0 (2 d), 127.1 (2 d), 129.4 (2 d), 132.6 (2 d), 134.2 (s), 134.9 (s), 150.3 (s), 173.7 (s).

Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.27; H, 6.49; N, 10.04.

2-Methyl-2-(*o*-tolyl)-*N*-(*p*-tolyl)propanamide (8h)

Yield: 100 mg (76%); colorless needles; mp 74–75 °C (EtOAc–hexane).

IR (KBr): 3340, 1665, 1595, 1515, 1400, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.65 (s, 6 H, 2 × CH_3), 2.28 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 6.80 (br s, 1 H, NH), 7.07 (d, *J* = 8.2 Hz, 2 H, ArH), 7.18–7.31 (m, 5 H, ArH), 7.47–7.51 (m, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.3 (q), 20.8 (q), 26.9 (2 q), 47.8 (s), 119.8 (2 d), 126.1 (d), 126.4 (d), 127.6 (d), 129.4 (2 d), 132.4 (d), 133.8 (s), 135.5 (s), 137.3 (s), 142.2 (s), 176.4 (s).

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.71; H, 7.95; N, 5.21.

2-(2-Chlorophenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8i)

Yield: 131 mg (87%); colorless needles; mp 101–102 °C (EtOAc–hexane).

IR (KBr): 3300, 1605, 1595, 1515, 1380, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.73 (s, 6 H, 2 × CH_3), 2.28 (s, 3 H, CH_3), 6.77 (br s, 1 H, NH), 7.08 (d, *J* = 8.3 Hz, 2 H, ArH), 7.19 (td, *J* = 7.7, 1.5 H, 1 H, ArH), 7.26 (d, *J* = 8.3 Hz, 2 H, ArH), 7.40 (td, *J* = 7.7, 1.2 Hz, 1 H, ArH), 7.57 (dd, *J* = 7.7, 1.5 Hz, 1 H, ArH), 7.63 (dd, *J* = 7.7, 1.2 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 26.6 (2 q), 49.3 (s), 120.3 (2 d), 124.5 (s), 128.0 (d), 128.3 (d), 129.1 (d), 129.3 (2 d), 133.8 (s), 135.2 (d), 135.5 (s), 143.0 (s), 174.6 (s).

Anal. Calcd for $C_{17}H_{18}ClNO$: C, 70.95; H, 6.30; N, 4.87. Found: C, 70.95; H, 6.36; N, 4.87.

2-(2-Bromophenyl)-2-methyl-*N*-(*p*-tolyl)propanamide (8j)

Yield: 132 mg (84%); colorless crystals; mp 108–109 °C (EtOAc–hexane).

IR (KBr): 3300, 1665, 1595, 1515, 1470, 1315 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.73 (s, 6 H, 2 × CH_3), 2.28 (s, 3 H, CH_3), 6.75 (br s, 1 H, NH), 7.08 (d, *J* = 8.3 Hz, 2 H, ArH), 7.20 (td, *J* = 7.7, 1.5 Hz, 1 H, ArH), 7.26 (d, *J* = 8.3 Hz, 2 H, ArH), 7.40 (td, *J* = 7.7, 1.2 Hz, 1 H, ArH), 7.57 (dd, *J* = 7.7, 1.5 Hz, 1 H, ArH), 7.64 (dd, *J* = 7.7, 1.2 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (q), 26.6 (2 q), 49.3 (s), 120.4 (2 d), 124.5 (s), 128.0 (d), 128.3 (d), 129.1 (d), 129.3 (2 d), 133.9 (s), 135.2 (d), 135.5 (s), 143.0 (s), 174.6 (s).

Anal. Calcd for $C_{17}H_{18}BrNO$: C, 61.46; H, 5.46; N, 4.22. Found: C, 61.43; H, 5.47; N, 4.21.

Acknowledgment

We are grateful to the National Science Council of ROC for financial support (Grant No. MOST-104-2113-M-006-003).

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588642.

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