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$Sc(OTf)_3$-Catalyzed Synthesis of Indoles and $SnCl_4$-Mediated Regioselective Hydrochlorination of 5-(Arylamino)pent-3-yn-2-ones

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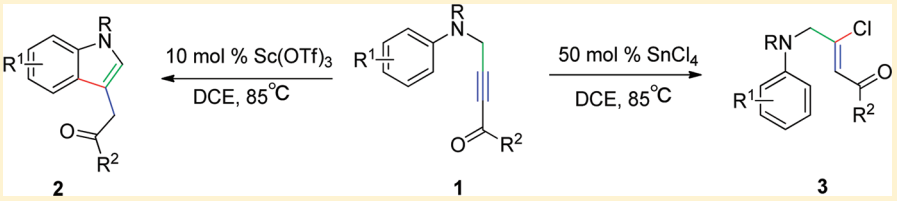
Supporting Information

ABSTRACT:



Highly substituted indole derivatives bearing alkyl and aryl moieties can be prepared by $Sc(OTf)_3$-catalyzed Friedel–Crafts alkenylation of 5-(arylamino)pent-3-yn-2-ones. In addition, a method for regioselective hydrochlorination of 5-(arylamino)pent-3-yn-2-ones mediated by $SnCl_4$ in moderate to good yields (up to 84%) has been developed. The resulting exclusive *Z*-selectivity of the C–Cl bond can be further exploited using cross C–N coupling reactions.

INTRODUCTION

The indole skeleton is a ubiquitous bioactive heterocycle in nature, especially in naturally occurring alkaloids. Indoles are often used for the construction of many biologically active compounds with diverse pharmacological properties,[1] such as Sumatriptan, ondansetron, and tadalafil.[2] Their important biological and pharmaceutical relevance has stimulated considerable interest of synthetic chemists and has encouraged the development of numerous synthetic strategies to prepare them. The structural core of indoles can be synthesized by various classical methods.[3] However, the functional group tolerance and the starting material availability often limit these syntheses. In some cases, it remains difficult to prepare suitably substituted indoles by standard indole-forming reactions. Thus, more benign protocols for preparing indoles from readily available and simple substrates still need to be actively persued. In recent years, a range of synthetic approaches to indoles have been reported,[4] in most of which the formation of the N–C2,[5] C2–C3,[6] or C3–C3a[7] bond is the key step. Lewis-acid-catalyzed or mediated methods have also been proven to be useful for preparing indoles.[8] We envisioned that the treatment of 5-(arylamino)pent-3-yn-2-ones **1** with Lewis acid would lead to intramolecular Friedel–Crafts reaction,[9] resulting in a quinoline derivative. However, unexpectedly, the final data revealed indole derivatives **2**. Herein, we report a $Sc(OTf)_3$-catalyzed[10] C–C bond formation for the synthesis of highly substituted indole derivatives using 5-(arylamino)pent-3-yn-2-ones as the substrates. Also, highly *Z*-selective C–Cl bond formation was also achieved in the presence of $SnCl_4$[11] as mediator.

RESULTS AND DISCUSSION

Our initial investigation was focused on finding a metal triflate[10a,b,12] catalyst to construct indole derivatives. Using 0.3 mmol of 4-((4-chlorophenyl)(methyl)amino)-1-phenylbut-2-yn-1-one **1a** and 5 mol % of $Sc(OTf)_3$ in 1,2-dichloroethane (DCE) at 60 °C, the desired product 2-(5-chloro-1-methyl-1*H*-indol-3-yl)-1-phenylethanone **2a** was formed in 35% yield after 24 h (Table 1, entry1). Other triflate salts, such as $Bi(OTf)_3$, $Hf(OTf)_4$, $In(OTf)_3$, $Yb(OTf)_3$, $Cu(OTf)_2$, and AgOTf, were also applied to the reaction, but these catalysts were found to be inefficient (entries 2–7). By increasing temperature to 85 °C, a 40% yield of **2a** was obtained (entry 8). With 10 mol % of $Sc(OTf)_3$, a moderate yield (51%) of **2a** was obtained after 24 h at 85 °C (entry 9). Other solvents were also tested in this reaction, but no superior results were obtained (entries 11–13). Other Lewis acid catalysts, such as TfOH, $BF_3 \cdot Et_2O$, $SnCl_4$, $TiCl_4$, $AuCl_3$, $FeCl_3$, and $AlCl_3$, were found to be inefficient to form indole derivatives. To our surprise, when 10 mol % of $SnCl_4$ was used as catalyst, a highly *Z*-selective C–Cl bond was constructed successfully. Then we increased the amount of $SnCl_4$ to 50 mol % (0.5 equiv), and a 60% yield of (*Z*)-3-chloro-4-((4-chlorophenyl)(methyl)amino)-1-phenylbut-2-en-1-one **3a** was obtained after 5 h (Table 1, entry 18). Other MCl_x salts were also tested, but no better results were obtained (entries 20–23).

To expand the scope of these divergent reactions of 5-(arylamino)pent-3-yn-2-ones, we first examined various representative 5-(arylamino)pent-3-yn-2-ones **1a–s** under indole-forming

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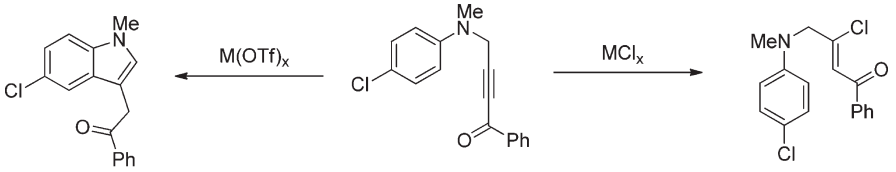
Table 1. Optimization of Conditions for the Transformation of 5-(Arylamino)pent-3-yn-2-ones 1a to Indole Derivatives 2a and (*Z*)-4-Chloropent-3-en-2-ones 3a



2a **1a** **3a**

					yield (%)	
entry	catalyst	solvent	temp (°C)	time (h)	**2a**	**3a**
1	$Sc(OTf)_3$ (5 mol %)	DCE	60	24	35	
2	$Bi(OTf)_3$ (5 mol %)	DCE	60	24	*a*	
3	$Hf(OTf)_4$ (5 mol %)	DCE	60	24	15	
4	$In(OTf)_3$ (5 mol %)	DCE	60	30	trace	
5	$Yb(OTf)_3$ (5 mol %)	DCE	60	24	10	
6	$Cu(OTf)_2$ (5 mol %)	DCE	60	24	*a*	
7	AgOTf (5 mol %)	DCE	60	24	*a*	
8	$Sc(OTf)_3$ (5 mol %)	DCE	85	24	40	
9	$Sc(OTf)_3$ (10 mol %)	DCE	85	24	51	
10	$Sc(OTf)_3$ (10 mol %)	DCE	100	24	43	
11	$Sc(OTf)_3$ (10 mol %)	CH_3CN	85	24	*a*	
12	$Sc(OTf)_3$ (10 mol %)	1,4-dioxane	85	24	15	
13	$Sc(OTf)_3$ (10 mol %)	toluene	85	24	45	
14	HOTf (10 mol %)	DCE	85	5	*a*	
15	$BF_3 \cdot Et_2O$ (10 mol %)	DCE	85	5	*a*	
16	$SnCl_4$ (10 mol %)	DCE	85	5	*a*	15
17	$SnCl_4$ (30 mol %)	DCE	85	5	*a*	52
18	$SnCl_4$ (50 mol %)	DCE	85	5	*a*	60
19	$SnCl_4$ (100 mol %)	DCE	85	5	*a*	45
20	$TiCl_4$ (50 mol %)	DCE	85	5	*a*	*b*
21	$AuCl_3$ (50 mol %)	DCE	85	5	*a*	58
22	$FeCl_3$ (50 mol %)	DCE	85	5	*a*	trace
23	$AlCl_3$ (50 mol %)	DCE	85	5	*a*	20

[a] No desired product was observed. [b] Decomposed.

conditions, as depicted in Scheme 1. Thus, the cascade reaction involving C−C bond formation of 5-(arylamino)pent-3-yn-2-ones **1a**−**s** proceeded smoothly to provide corresponding products **2a**−**s** in moderate to good yields. When the R^2 is a phenyl group, the reaction works well with both electron-donating and electron-withdrawing R^1 groups (Scheme 1, **2a**−**2i**). Moderate yields of corresponding products were obtained with little effect shown by R groups to this transformation. Substrate **1j** with an electron-withdrawing aryl R^2 group, such as 4-ClC_6H_4, and an electron-withdrawing R^1 group (4-Cl) can afford the desired product **2m** in 63% yield. The derivative **1m** can also give the expected indole **2m** in 81% yield. Furthermore, to expand the scope of this reaction, we also investigated a range of 5-(arylamino)pent-3-yn-2-ones **1n**−**q**. Under the optimized condition, several 1*H*-benzo[*g*]indole derivatives **2n**−**q** can be prepared successfully in moderate yields. The molecular structure of the representative product **2q** was determined by X-ray crystallography (see Supporting Information).[13] To our delight, when 5-(arylamino)pent-3-yn-2-ones **1r**,**s** were subjected to this transformation, the corresponding 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline derivatives **2r**,**s**, which are important intermediates in natural products, were separated in moderate yields.

After this, we examined the scope of C−Cl bond formation of 5-(arylamino)pent-3-yn-2-ones. Under the optimized condition, we also investigated a wide range of 5-(arylamino)pent-3-yn-2-ones **1** with different substituents R, R^1, and R^2 in the presence of 0.5 equiv of $SnCl_4$ at 85 °C in DCE. It was found that these substrates were effectively converted into the corresponding (*Z*)-4-chloropent-3-en-2-ones **3** in moderate to good yield with exclusive *Z*-selectivity, as depicted in Table 2. The molecular structure of the representative product **3l** was determined by X-ray crystallography (see Supporting Information).[14] The reaction tolerates the presence of different electron-donating and electron-withdrawing aryl groups. Fortunately, in all of the examples studied, only exclusive *Z*-selective products were obtained.

A standard feature of this process is the fact that the (*Z*)-4-chloropent-3-en-2-ones mediated by $SnCl_4$ can be further elaborated by using various copper-catalyzed processes. For example, the Ullmann coupling of (*Z*)-4-chloropent-3-en-2-ones **3l** afforded the corresponding product **4l** in moderate yield (Scheme 2).

On the basis of the above observations, we propose the following plausible mechanisms for $Sc(OTf)_3$-catalyzed and $SnCl_4$-mediated

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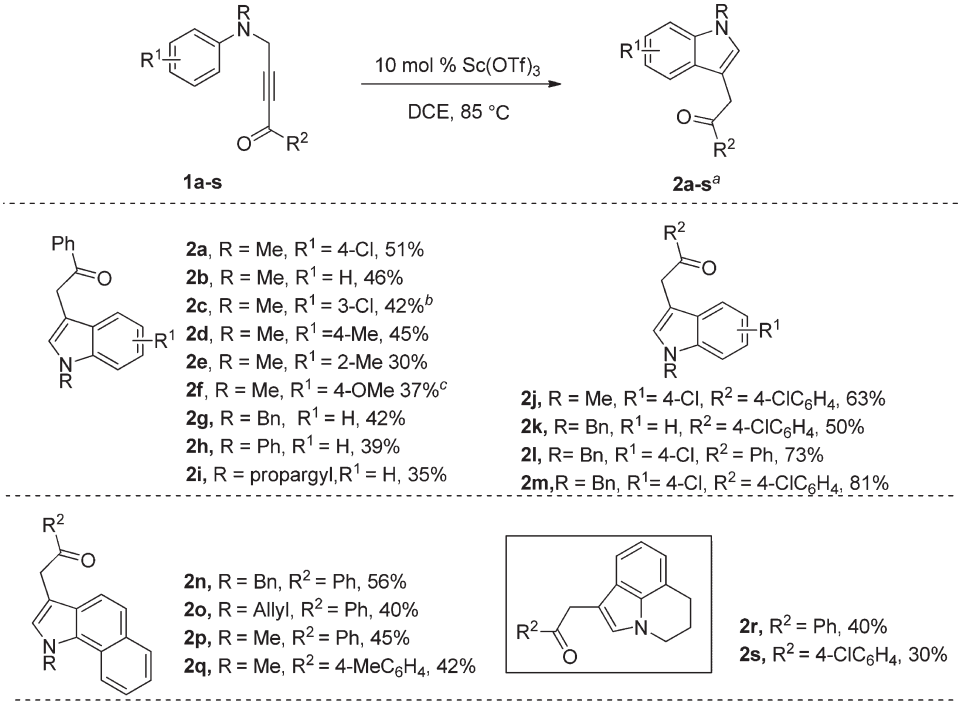
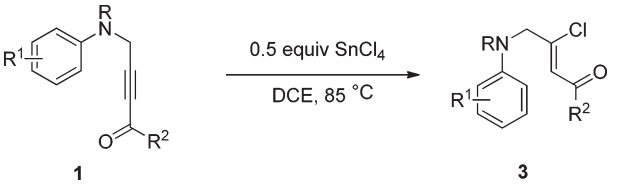
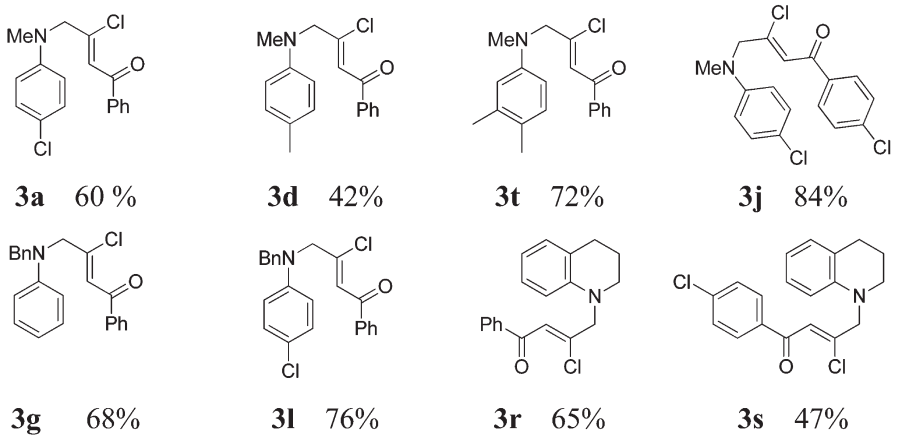
Scheme 1. $Sc(OTf)_3$-Catalyzed C−C Bond Formation of 5-(Arylamino)pent-3-yn-2-ones 1 to Indole Derivatives 2[a]



[a] Conditions: 0.3 mmol of **1** with 10 mol % of $Sc(OTf)_3$ in DCE (3.0 mL) at 85 °C. [b] For details, see the Supporting Information. [c] The reaction was carried out in toluene at 85 °C.

Table 2. $SnCl_4$-Mediated Regioselective formation of (Z)-4-Chloropent-3-en-2-ones 3 from 5-(Arylamino)pent-3-yn-2-ones 1[a]





[a] Conditions: 0.3 mmol of **1** with 0.5 equiv of $SnCl_4$ in DCE (3.0 mL) at 85 °C.

cascade reactions (Scheme 3), which may involve the following steps. (i) Coordination of the carbonyl moiety of 5-(arylamino)pent-3-yn-2-ones **1** to $Sc(OTf)_3$ catalyst gives the complex **A**. (ii) The subsequent *ortho*-carbon atom of arylamine as the nucleophile attacks the carbon−carbon triple bond and affords intermediate **B**. (iii) **B** on isomerization yields

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1-(indolin-3-ylidene)propan-2-one **C** and regenerates the catalyst $Sc(OTf)_3$. (iv) **C** undergoes the subsequent 1,3-H shift to give indole derivatives **2**. (v) $SnCl_4$ eliminates a chloride anion to give $SnCl_3$, which coordinates with the carbonyl moiety of 5-(arylamino)pent-3-yn-2-ones **1** to give complex **D**.[11a,b] (vi) The chlorine anion as nucleophile attacks the carbon−carbon triple bond and affords intermediate trichloro((3-chloropropa-1,2-dien-1-yl)oxy)stannane **E**. (vii) **E** is hydrolyzed and isomerization to give *Z*-selective products **3**, during which the steric effect plays a key role. Meanwhile, the $SnCl_{4-n}(OH)_n$[11c] can mediate the reaction again by eliminating a second chloride anion.

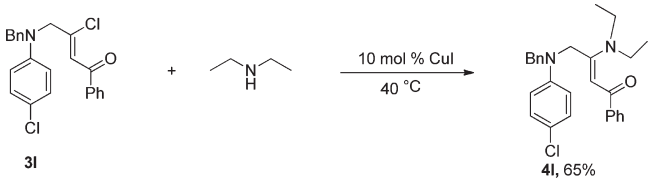
CONCLUSION

In summary, a $Sc(OTf)_3$-catalyzed intramolecular Friedel−Crafts reaction for the synthesis of highly substituted indole derivatives **2** from 5-(arylamino)pent-3-yn-2-ones **1** has been realized. In addition, a $SnCl_4$-mediated protocol for highly *Z*-selective C−Cl bond formation was also successfully developed. The resulting C−Cl bond can be further exploited using cross C−N coupling reactions.

EXPERIMENTAL SECTION

General Procedure: Synthesis of Indole Derivatives 2a−2s. To a solution of 5-(arylamino)pent-3-yn-2-ones **1** (0.20 mmol) in DCE (3.0 mL) was added 9.8 mg (10 mol %) of $Sc(OTf)_3$. The resulting mixture was stirred at 85 °C. When the reaction was considered complete as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (40 mL), washed with water and saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford corresponding 2-(1*H*-indol-3-yl)ethanones **2a**−**2s**.

Scheme 2. Cu-Catalyzed Ullmann Reaction of 3l to 4l



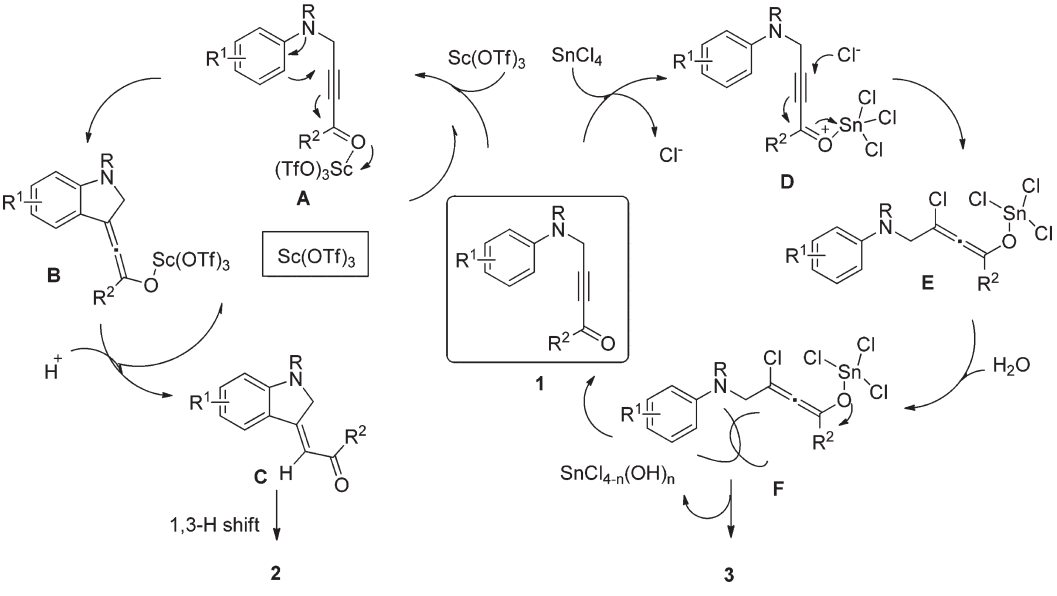
Characterization Data of 2a−s. *2-(5-Chloro-1-methyl-1H-indol-3-yl)-1-phenylethanone* ***2a****:* yield 51%; dark red solid; mp 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.2 Hz, 2H), 7.57−7.53 (m, 2H), 7.47−7.43 (m, 2H), 7.19−7.14 (m, 2H), 7.01 (s, 1H), 4.34 (s, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.4, 136.6, 135.3, 133.1, 129.2, 128.8, 128.6, 128.5, 125.1, 122.1, 118.4, 110.4, 106.9, 35.1, 32.9; IR (neat, cm^{-1}) 2923, 1724, 1683, 1477, 1451, 1211, 792, 690; HRMS (ESI) calcd for $C_{17}H_{14}ClNO$ $[M + H]^+$ = 284.0837, found 284.0841.

2-(1-Methyl-1H-indol-3-yl)-1-phenylethanone ***2b****:* yield 46%; dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 6.8 Hz, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.51−7.47 (m, 1H), 7.39 (t, J = 7.6 Hz, 2H), 7.24−7.18 (m, 2H), 7.13−7.09 (m, 1H), 6.94 (s, 1H), 4.35 (s, 2H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.8, 136.8, 136.6, 132.9, 128.5, 128.5, 127.8, 127.7, 121.7, 119.1, 118.8, 109.2, 107.1, 35.3, 32.6; IR (neat, cm^{-1}) 2924, 1679, 1596, 1473, 1448, 1332, 1210, 742, 689; HRMS (ESI) calcd for $C_{17}H_{15}NO$ $[M + H]^+$ = 250.1226, found 250.1228.

2-(4-Chloro-1-methyl-1H-indol-3-yl)-1-phenylethanone ***2c′*** *Compound with 2-(6-Chloro-1-methyl-1H-indol-3-yl)-1-phenylethanone* ***2c″*** *(1:1):* yield 42%; dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 1.2 Hz, 2H), 8.03 (d, J = 8.0 Hz, 2H), 7.58−7.52 (m, 2H), 7.49 (s, 3H), 7.47−7.42 (m, 2H), 7.26 (d, J = 2.0 Hz, 1H), 7.18 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 7.09−7.02 (m, 3H), 6.98 (s, 2H), 4.69 (s, 2H), 4.35 (s, 2H), 3.71 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 198.3, 197.5, 138.4, 137.3, 137.0, 136.6, 133.1, 132.9, 129.5, 128.6, 128.6, 128.5, 128.5, 128.4, 127.9, 126.4, 126.2, 124.4, 122.1, 120.1, 119.9, 119.8, 109.4, 108.2, 107.5, 107.5, 36.3, 35.2, 33.0, 32.8; IR (neat, cm^{-1}) 2926, 1687, 1600, 1476, 1452, 1331, 1212, 1067, 757, 691; HRMS (ESI) calcd for $C_{17}H_{14}ClNO$ $[M + H]^+$ = 284.0837, found 284.0847.

2-(1,5-Dimethyl-1H-indol-3-yl)-1-phenylethanone ***2d****:* yield 45%; dark red oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 6.9 Hz, 1H), 7.38−7.31 (m, 3H), 7.09 (d, J = 8.1 Hz, 1H), 6.97 (d, J = 8.1 Hz, 1H), 6.86 (s, 1H), 4.29 (s, 2H), 3.62 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 197.9, 136.7, 135.3, 132.9, 128.6, 128.5, 128.4, 127.9, 123.4, 118.4, 109.0, 106.6, 35.5, 32.7, 21.5; IR

Scheme 3. Proposed Mechanism



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(neat, cm^{-1}) 2360, 1629, 1531, 1218, 768, 689; HRMS (ESI) calcd for $C_{18}H_{17}NO$ $[M + H]^+$ = 264.1383, found 264.1389.

2-(1,7-Dimethyl-1H-indol-3-yl)-1-phenylethanone ***2e***: yield 30%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.44−7.41 (m, 3H), 6.98 (t, J = 7.2 Hz, 1H), 6.90 (d, J = 7.2 Hz, 1H), 6.86 (s, 1H), 4.34 (s, 2H), 3.97 (s, 3H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.9, 136.7, 135.6, 132.9, 129.4, 128.8, 128.6, 128.5, 124.4, 121.3, 119.5, 116.8, 107.0, 36.6, 35.3, 19.6; IR (neat, cm^{-1}) 2922, 1670, 1382, 1069, 752, 689; HRMS (ESI) calcd for $C_{18}H_{17}NO$ $[M + H]^+$ = 264.1383, found 264.1389.

2-(5-Methoxy-1-methyl-1H-indol-3-yl)-1-phenylethanone ***2f***: yield 37%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−8.03 (m, 2H), 7.54−7.50 (m, 1H), 7.48 (s, 1H), 7.46−7.41 (m, 2H), 6.86 (s, 1H), 6.79 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 6.73 (d, J = 2.0 Hz, 1H), 4.34 (s, 2H), 3.86 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.8, 156.5, 137.6, 136.7, 132.9, 128.6, 128.5, 126.6, 122.2, 119.6, 109.1, 107.3, 92.9, 55.7, 35.5, 32.7; IR (neat, cm^{-1}) 2921, 1669, 1611, 1499, 1219, 1055, 772, 691; HRMS (ESI) calcd for $C_{18}H_{17}$ NO $[M + H]^+$ = 280.1332, found 280.1336.

2-(1Benzyl-1H-indol-3-yl)-1-phenylethanone ***2g***: yield 42%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06−8.04 (m, 2H), 7.63 (d, J = 7.2 Hz, 1H), 7.55−7.51 (m, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.24−7.21 (m, 3H), 7.19−7.11 (m, 3H), 7.08−7.05 (m, 3H), 5.26 (s, 2H), 4.41 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.8, 137.4, 136.7, 136.5, 132.9, 128.7, 128.6, 128.5, 128.0, 127.5, 127.3, 126.7, 122.0, 119.5, 119.0, 109.8, 108.1, 50.0, 35.6; IR (neat, cm^{-1}) 2923, 2360, 1678, 1601, 1449, 1174, 746, 695; HRMS (ESI) calcd for $C_{23}H_{19}NO$ $[M + H]^+$ = 326.1539, found 326.1543.

1-Phenyl-2-(1-phenyl-1H-indol-3-yl)ethanone ***2h***: yield 39%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.54 (t, J = 7.2 Hz, 2H), 7.47−7.43 (m, 6H), 7.33−7.30 (m, 2H), 7.25−7.17 (m, 2H), 4.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.5, 139.6, 136.6, 136.0, 133.1, 129.5, 128.8, 128.6, 128.5, 126.9, 126.3, 124.2, 122.7, 120.3, 119.2, 110.6, 110.0, 35.4; IR (neat, cm^{-1}) 2921, 1683, 1596, 1500, 1455, 1210, 749, 695; HRMS (ESI) calcd for $C_{22}H_{17}$ NO $[M + H]^+$ = 312.1383, found 312.1389.

1-Phenyl-2-(1-(prop-2-yn-1-yl)-1H-indol-3-yl)ethanone ***2i***: yield 35%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.4 Hz, 1H), 7.25−7.23 (m, 1H), 7.16−7.14 (m, 2H), 4.81 (d, J = 2.0 Hz, 2H), 4.39 (s, 2H), 1.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.6, 136.7, 136.1, 133.0, 128.6, 128.6, 128.3, 126.3, 122.2, 119.8, 119.1, 109.4, 108.5, 77.7, 73.5, 35.7, 35.4; IR (neat, cm^{-1}) 2922, 1681, 1598, 1466, 1337, 1211, 1181, 745, 689; HRMS (ESI) calcd for $C_{19}H_{15}NO$ $[M + H]^+$ = 274.1226, found 274.1230.

2-(5-Chloro-1-methyl-1H-indol-3-yl)-1-(4-chlorophenyl)ethanone ***2j***: yield 63%; dark red solid; mp 190−192 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.8 Hz, 2H), 7.52 (t, J = 0.8 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.19−7.16 (m, 2H), 6.99 (s, 1H), 4.29 (s, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 196.2, 139.5, 135.3, 134.8, 129.9, 129.2, 128.9, 128.7, 125.2, 122.1, 118.3, 110.4, 106.6, 35.2, 32.9; IR (neat, cm^{-1}) 2922, 2361, 2336, 1679, 1091, 785, 671; HRMS (ESI) calcd for $C_{17}H_{13}Cl_2NO$ $[M + H]^+$ = 318.0447, found 318.0450.

2-(1-Benzyl-1H-indol-3-yl)-1-(4-chlorophenyl)ethanone ***2k***: yield 50%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.24 (s, 3H), 7.19−7.11 (m, 3H), 7.06−7.04 (m, 3H), 5.25 (s, 2H), 4.36 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 196.6, 139.3, 137.4, 136.6, 134.9, 130.0, 128.8, 128.7, 127.9, 127.6, 127.2, 126.7, 122.1, 119.6, 118.9, 109.9, 107.8, 50.0, 35.7; IR (neat, cm^{-1}) 2923, 2361, 1679, 1589, 1393, 1171, 1092, 741, 699; HRMS (ESI) calcd for $C_{23}H_{18}ClNO$ $[M + H]^+$ = 360.1150, found 360.1158.

2-(1-Benzyl-5-chloro-1H-indol-3-yl)-1-phenylethanone ***2l***: yield 73%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.57−7.54 (m, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.26−7.23 (m, 3H), 7.15−7.11 (m, 3H), 7.05−7.03 (m, 2H), 5.24 (s, 2H), 4.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.3, 137.0, 136.6, 134.9, 133.1, 129.2, 128.8, 128.7, 128.6, 128.5, 127.7, 126.7, 125.4, 122.3, 118.6, 110.9, 107.7, 50.2, 35.3; IR (neat, cm^{-1}) 2923, 1685, 1470, 1448, 1211, 772, 694; HRMS (ESI) calcd for $C_{23}H_{18}ClNO$ $[M + H]^+$ = 360.1150, found 360.1153.

2-(1-Benzyl-5-chloro-1H-indol-3-yl)-1-(4-chlorophenyl)ethanone ***2m***: yield 81%; dark red solid; mp 74−76 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.8 Hz, 2H), 7.55 (d, J = 1.6 Hz, 1H), 7.41 (d, J = 8.8 Hz, 2H), 7.30−7.26 (m, 3H), 7.16−7.10 (m, 2H), 7.09 (s, 1H), 7.05−7.03 (m, 2H), 5.24 (s, 2H), 4.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 196.1, 139.5, 136.9, 135.0, 134.8, 129.9, 129.0, 128.9, 128.8, 128.7, 127.8, 126.7, 125.5, 122.4, 118.5, 110.9, 107.4, 50.2, 35.4; IR (neat, cm^{-1}) 2923, 1689, 1588, 1470, 1204, 1092, 772, 733, 699; HRMS (ESI) calcd for $C_{23}H_{17}Cl_2NO$ $[M + H]^+$ = 394.0760, found 394.0766.

2-(1-Benzyl-1H-benzo[g]indol-3-yl)-1-phenylethanone ***2n***: yield 56%; dark red solid; mp 66−68 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.2 Hz, 2H), 8.01 (d, J = 7.6 Hz, 1H), 7.88 (d, J = 7.2 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.55−7.52 (m, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.34−7.29 (m, 2H), 7.28−7.19 (m, 3H), 7.09 (s, 1H), 7.00 (d, J = 6.4 Hz, 2H), 5.70 (s, 2H), 4.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.8, 137.6, 136.7, 133.0, 131.4, 129.9, 129.1, 128.9, 128.6, 128.5, 128.1, 127.4, 125.9, 125.3, 125.2, 123.4, 122.6, 121.3, 120.9, 118.7, 109.1, 53.4, 35.5; IR (neat, cm^{-1}) 2089, 1637, 802, 745; HRMS (ESI) calcd for $C_{27}H_{21}NO$ $[M + H]^+$ = 376.1690, found 376.1694.

2-(1-Allyl-1H-benzo[g]indol-3-yl)-1-phenylethanone ***2o***: yield 40%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 7.2 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.55−7.50 (m, 2H), 7.48−7.44 (m, 2H), 7.42−7.38 (m, 2H), 7.05 (s, 1H), 6.19−6.10 (m, 1H), 5.22 (d, J = 10.8 Hz, 1H), 5.11 (t, J = 2.4 Hz, 2H), 4.91 (d, J = 17.2 Hz, 1H), 4.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.8, 136.7, 133.6, 133.0, 131.4, 129.7, 129.2, 128.6, 128.5, 127.5, 125.2, 125.0, 123.4, 122.6, 121.1, 121.1, 118.7, 117.2, 108.9, 52.1, 35.5; IR (neat, cm^{-1}) 2922, 1681, 809, 747; HRMS (ESI) calcd for $C_{23}H_{19}NO$ $[M + H]^+$ = 326.1539, found 326.1545.

2-(1-Methyl-1H-benzo[g]indol-3-yl)-1-phenylethanone ***2p***: yield 45%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 7.2 Hz, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.54−7.48 (m, 3H), 7.41 (q, J = 7.6 Hz, 3H), 6.97 (s, 1H), 4.43 (s, 2H), 4.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.8, 136.7, 133.0, 131.4, 130.2, 129.2, 128.6, 128.6, 128.1, 125.2, 124.8, 123.3, 120.8, 120.6, 118.7, 108.1, 38.3, 35.3; IR (neat, cm^{-1}) 2922, 2361, 2336, 1680, 1394, 1068, 689; HRMS (ESI) calcd for $C_{21}H_{17}NO$ $[M + H]^+$ = 300.1383, found 300.1377.

2-(1-Methyl-1H-benzo[g]indol-3-yl)-1-(p-tolyl)ethanone ***2q***: yield 42%; yellow solid; mp 146−148 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 8.4 Hz, 1H), 7.97−7.92 (m, 3H), 7.68 (d, J = 8.8 Hz, 1H), 7.52−7.48 (m, 2H), 7.43−7.39 (m, 1H), 7.23 (d, J = 8.4 Hz, 2H), 6.98 (s, 1H), 4.41 (s, 2H), 4.21 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.5, 143.7, 134.2, 131.4, 129.3, 129.2, 128.7, 128.1, 125.2, 124.9, 123.4, 123.3, 120.8, 120.6, 118.8, 108.4, 38.3, 35.3, 29.7, 21.6; IR (neat, cm^{-1}) 2922, 1677, 1605, 1397, 1284, 805, 748; HRMS (ESI) calcd for $C_{22}H_{19}NO$ $[M + H]^+$ = 314.15393, found 314.1545.

2-(5,6-Dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)-1-phenylethanone ***2r***: yield 40%; dark red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 8.0 Hz, 3H), 7.03 (t, J = 7.6 Hz, 2H), 6.90 (d, J = 9.2 Hz, 1H), 4.39 (s, 2H), 4.09(t, J = 6.0 Hz, 2H), 2.96 (t, J = 6.0 Hz, 2H), 2.23−2.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 197.9, 136.7, 134.4, 132.9, 128.6, 128.5, 125.3, 125.1, 121.7, 119.6, 118.6, 116.3, 107.2, 43.9, 35.8, 24.6, 22.8; IR (neat, cm^{-1}) 2930, 1679, 1626, 1448, 1213, 752; HRMS (ESI) calcd for $C_{19}H_{17}NO$ $[M + H]^+$ = 276.1383, found 276.1386.

1-(4-Chlorophenyl)-2-(5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl) ethanone ***2s***: yield 30%; dark red solid; mp 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 2H), 7.40−7.37 (m, 3H), 7.04 (t, J = 7.6 Hz, 1H), 6.98 (s, 1H), 6.91 (d, J = 6.8 Hz, 1H), 4.35 (s, 2H), 4.09 (t, J = 5.6 Hz, 2H), 2.96 (t, J = 6.0 Hz, 2H), 2.23−2.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 196.7, 139.3, 135.0, 130.1, 128.8, 125.1, 125.0, 121.8, 119.7, 118.7, 116.2, 106.8, 44.0, 35.9, 29.7, 24.6, 22.8; IR (neat, cm^{-1}) 2927, 1684, 1627, 1591, 1390, 1091, 750; HRMS (ESI) calcd for $C_{19}H_{16}$ ClNO [M + H] = 310.0993, found 310.0999.

General Procedure: Synthesis of (*Z*)-4-Chloropent-3-en-2-ones 3. To a solution of 5-(arylamino)pent-3-yn-2-ones **1** (0.20 mmol) in DCE (3.0 mL) was added $SnCl_4$ (0.5 equiv). The resulting mixture was stirred at 85 °C. When the reaction was considered complete as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (40 mL), washed with water and saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford corresponding (*Z*)-4-chloropent-3-en-2-ones **3**.

Characterization Data of 3a−3t. *(Z)-3-Chloro-4-((4-chlorophenyl)-(methyl)amino)-1-phenylbut-2-en-1-one* ***3a***: yield 60%; dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.74 (m, 2H), 7.57−7.52 (m, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.25−7.23 (m, 2H), 6.84 (t, J = 1.6 Hz, 1H), 6.70−6.66 (m, 2H), 4.20 (d, J = 1.6 Hz, 2H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.5, 146.6, 141.6, 137.2, 133.4, 129.2, 128.7, 128.5, 122.7, 120.7, 113.3, 60.5, 39.1; IR (neat, cm^{-1}) 2917, 1670, 1598, 1501, 1217, 811, 764, 695; HRMS (ESI) calcd for $C_{17}H_{15}Cl_2NO$ $[M + H]^+$ = 320.0603, found 320.0608.

(Z)-3-Chloro-4-(methyl(p-tolyl)amino)-1-phenylbut-2-en-1-one ***3d***: yield 42%; dark red oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 8.1 Hz, 2H), 7.46 (t, J = 7.2 Hz, 1H), 7.35−7.30 (m, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 1.2 Hz, 1H), 6.61 (d, J = 8.4 Hz, 2H), 4.11 (s, 2H), 3.02 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 189.7, 146.0, 142.5, 133.3, 129.9, 129.6, 128.6, 128.5, 127.0, 120.5, 112.3, 60.8, 38.9, 20.2; IR (neat, cm^{-1}) 2922, 1669, 1616, 1518, 1449, 1258, 1219, 805, 756, 696; HRMS (ESI) calcd for $C_{18}H_{18}$ClNO $[M + H]^+$ = 300.1150, found 300.1156.

(Z)-4-(Benzyl(phenyl)amino)-3-chloro-1-phenylbut-2-en-1-one ***3g***: yield 68%; dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.2 Hz, 2H), 7.30−7.27 (m, 4H), 6.70 (s, 1H), 6.84−6.79 (m, 3H), 4.71 (s, 2H), 4.30 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.7, 147.6, 141.9, 137.6, 137.3, 133.3, 129.5, 128.8, 128.6, 127.3, 126.7, 120.9, 118.1, 112.6, 58.4, 54.4; IR (neat, cm^{-1}) 2360, 1641, 1502, 747, 694; HRMS (ESI) calcd for $C_{23}H_{20}$ClNO $[M + H]^+$ = 362.1306, found 362.1310.

(Z)-3-Chloro-1-(4-chlorophenyl)-4-((4-chlorophenyl)(methyl)amino) but-2-en-1-one ***3j***: yield 84%; dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.8 Hz, 2H), 7.24 (d, J = 9.2 Hz), 7.12 (d, J = 8.8 Hz, 2H), 6.79 (s, 1H), 6.67 (d, J = 8.8 Hz, 2H), 4.19 (d, J = 1.6 Hz, 2H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 188.3, 146.6, 142.3, 139.9, 135.5, 129.9, 129.3, 129.0, 122.8, 120.3, 113.3, 60.5, 39.1; IR (neat, cm^{-1}) 2921, 2361, 2336, 1671, 1594, 1501, 1216, 1093, 813; HRMS (ESI) calcd for $C_{17}H_{14}Cl_3NO$ [M + H]$^+$ = 354.0214, found 354.0220.

(Z)-4-(Benzyl(4-chlorophenyl)amino)-3-chloro-1-phenylbut-2-en-1-one ***3l***: yield 76%; yellow solid; mp 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 8.0 Hz, 2H), 7.37−7.33 (m, 2H), 7.28 (t, J = 7.2 Hz, 1H), 7.24−7.17 (m, 4H), 6.95 (s, 1H), 6.70 (d, J = 9.2 Hz, 2H), 4.67 (s, 2H), 4.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.5, 146.1, 141.5, 137.1, 137.0, 133.4, 129.3, 128.9, 128.7, 128.5, 127.4, 126.5, 123.0, 120.9, 113.7, 58.5, 54.5; IR (neat, cm^{-1}) 2924, 1671, 1598, 1499, 1261, 1225, 811, 733, 697; HRMS (ESI) calcd for $C_{23}H_{19}Cl_2NO$ $[M + H]^+$ = 396.0916, found 396.0920.

(Z)-3-Chloro-4-(3,4-dihydroquinolin-1(2H)-yl)-1-phenylbut-2-en-1-one ***3r***: yield 65%; yellow solid; mp 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.11 (t, J = 7.6 Hz, 1H), 7.01 (t, J = 7.2 Hz, 2H), 6.69 (t, J = 7.6 Hz, 1H), 6.55 (d, J = 8.0 Hz, 1H), 4.15 (s, 2H), 3.44 (t, J = 6.0 Hz, 2H), 2.83 (t, J = 6.2 Hz, 2H), 2.07−2.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.9, 143.9, 142.0, 137.3, 133.3, 129.3, 128.6, 127.4, 122.5, 120.3, 117.2, 111.0, 59.4, 50.4, 27.9, 22.4; IR (neat, cm^{-1}) 2926, 1670, 1602, 1501, 1218, 748, 696; HRMS (ESI) calcd for $C_{19}H_{18}$ClNO $[M + H]^+$ = 312.1150, found 312.1156.

(Z)-3-Chloro-1-(4-chlorophenyl)-4-(3,4-dihydroquinolin-1(2H)-yl)but-2-en-1-one ***3s***: yield 47%; orange solid; mp 78−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62, (d, J = 7.8 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.03 (t, J = 7.8 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 6.84 (s, 1H), 6.62 (t, J = 7.2 Hz, 1H), 6.45 (d, J = 8.4 Hz, 1H), 4.07 (s, 2H), 3.36 (t, J = 5.1 Hz, 2H), 2.75 (t, J = 6.6 Hz, 2H), 1.95 (q, J = 5.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 188.7, 143.8, 142.5, 139.8, 135.7, 130.0, 129.4, 129.0, 127.4, 122.6, 120.0, 117.3, 111.0, 59.4, 50.4, 27.9, 22.4; IR (neat, cm^{-1}) 2928, 2847, 1672, 1604, 1502, 1217, 1091, 853, 819, 748; HRMS (ESI) calcd for $C_{19}H_{17}Cl_2NO$ $[M + H]^+$ = 346.0760, found 346.0766.

(Z)-3-Chloro-4-((3,4-dimethylphenyl)(methyl)amino)-1-phenylbut-2-en-1-one ***3t***: yield 72%; dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.77 (m, 2H), 7.55−7.50 (m, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.4 Hz, 1H), 6.92 (t, J = 1.2 Hz, 1H), 6.58 (d, J = 2.4 Hz, 1H), 6.53 (dd, J = 8.0 Hz, 2.8 Hz, 1H), 4.17 (d, J = 1.2 Hz, 2H), 3.08 (s, 3H), 2.26 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 189.8, 146.5, 142.5, 137.5, 137.3, 133.2, 130.4, 128.6, 128.6, 125.8, 120.6, 113.9, 109.9, 60.8, 38.9, 20.3, 18.6; IR (neat, cm^{-1}) 2920, 2361, 2336, 1671, 1615, 1511, 1219, 1018, 774, 695; HRMS (ESI) calcd for $C_{19}H_{20}$ClNO $[M + H]^+$ = 314.1306, found 314.1312.

Characterization Data of 4l. *(Z)-4-(Benzyl(4-chlorophenyl)amino)-3-(diethylamino)-1-phenylbut-2-en-1-one* ***4l***: yield 65%; yellow solid; mp 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 2H), 7.44−7.38 (m, 3H), 7.23−7.19 (m, 2H), 7.18−7.15 (m, 5H), 6.82 (d, J = 8.8 Hz, 2H), 5.77 (s, 1H), 4.89 (s, 2H), 4.60 (s, 2H), 3.22 (q, J = 7.2 Hz, 4H), 0.99 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 188.0, 159.4, 149.0, 142.7, 140.2, 130.6, 129.0, 128.2, 128.1, 127.3, 126.7, 126.6, 123.1, 115.6, 95.0, 54.7, 45.8, 44.4, 12.4; IR (neat, cm^{-1}) 2977, 2928, 1535, 1491, 1355, 1222, 759, 703; HRMS (ESI) calcd for $C_{27}H_{29}ClN_2O$ $[M + H]^+$ = 433.2041, found 433.2047.

■ ASSOCIATED CONTENT

Supporting Information. Experimental details, analytical data for all new compounds, and X-ray crystallography data of **2p** and **3l** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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