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Buchwald–Hartwig Coupling/Michael Addition Reactions: One-Pot Synthesis of 1,2-Disubstituted 4-Quinolones from Chalcones and Primary Amines

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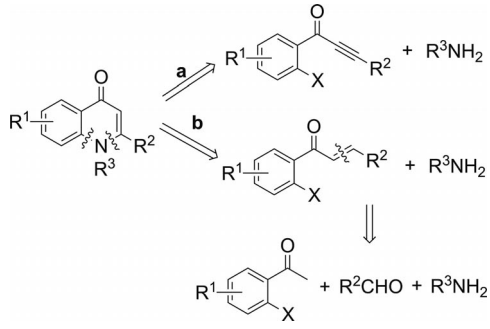
The Buchwald–Hartwig coupling/Michael addition sequence has been successfully applied to the synthesis of functionalized 1,2-disubstituted 4-quinolones using $Pd(OAc)_2$ as a catalyst and PPh_3 as a ligand. Under these conditions, the intermediate products first formed from chalcones and primary amines underwent catalytic dehydrogenation to yield the 1,2-disubstituted 4-quinolones.

Introduction

Over the years, 4-quinolone derivatives have attracted considerable attention from medicinal chemists due to their diverse biological activity. They have been extensively studied as a useful structural moiety for drug candidates. Some of them have been investigated as antiviral,[1] antimitotic,[2] antidiabetic,[3] antibacterial,[4] antitrypanosomal,[4b] and antitumor agents[5] as well as HIV-1 integrase inhibitors.[6] In addition, scientists have found that quinolone derivatives exhibit selective M1 positive allosteric modulating activity.[7] Such characteristics have made the molecule important and this has resulted in sustained interest in developing new efficient synthetic strategies for this structural moiety. Numerous synthetic routes to 4-quinolones have been reported involving Camps cyclization,[8] reaction of isatoic anhydrides,[9–12] cyclization of *N*-substituted phenacyl or acetonyl anthranilates in polyphosphoric acid,[13] cyclization of anthranilic acid derived ynone intermediates,[14] intramolecular coupling of aryl halides with β-enaminones,[15] acid-catalyzed cyclization,[16] cycloacylation of aniline derivatives,[17] palladium-catalyzed carbonylative Sonogashira coupling of 2-iodoaniline with arylacetylene,[18] and metal-free intramolecular amination.[19] Although these methods are effective and give relatively high yields, most of them give 1-unsubstituted 2-substituted 4-quinolones, 1-unsubstituted 3-substituted 4-quinolones, or 1,3-disubstituted 4-quinolones. Only a few literature reports give examples of 1,2-disubstituted 4-quinolone syntheses.

Recently, the synthesis of 1,2-disubstituted 4-quinolones has been reported by palladium-catalyzed tandem amination and copper-catalyzed cyclization.[20a,20b] However, the deficiency is that the alkynone substrates were synthesized from phenylacetylene by using *n*BuLi at –78 °C or $[PdCl_2(PPh)_3]$/CuI as catalysts, which increases the difficulty of substrate preparation (Scheme 1, a). On this basis, we considered investigating a more general strategy for the synthesis of 1,2-disubstituted 4-quinolones by using chalcones as substrates, which can be easily obtained by aldol condensation of the acetophenone with appropriate aldehydes (Scheme 1, b).



Scheme 1. Strategy for the synthesis of 1,2-disubstituted 4-quinolones.

Results and Discussion

During the course of our study we screened different combinations of catalysts, solvents, and bases in an effort to improve the yields. In an initial attempt, the reaction was performed with $Pd(OAc)_2$ as catalyst in the presence of K_2CO_3 as base in anhydrous dioxane (Table 1, entry 1). The product **3a** was not observed. However, the expected product **3a** was formed in 74% yield when PPh_3 was employed as a ligand in the reaction (Table 1, entry 2). The yields

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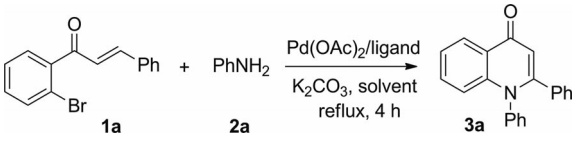
could not be improved by using other ligands such as PCy_3, DPPE, DPPF, and TFP (Table 1, entries 3–6). In comparison with K_2CO_3, the use of Cs_2CO_3 as base resulted in a lower yield (Table 1, entry 7). The effect of solvent was then explored, however, better results were not obtained with other solvents (Table 1, entries 8–11). When $[Pd_2(dba)_3]$ was used as catalyst and combined with PPh_3, the yield was slightly lower (Table 1, entry 12). Thus, the best result was obtained by using **1a** and aniline in the presence of $Pd(OAc)_2$ (5 mol-%) and PPh_3 (10 mol-%) in anhydrous dioxane (1 mL) with K_2CO_3 (2 equiv.) as base.

Table 1. Optimization of the reaction conditions for the synthesis of 1,2-disubstituted 4-quinolones.[a]



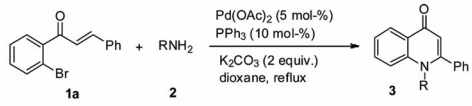
Entry	Ligand	Solvent	Temperature	Yield [%][b]
1	–	dioxane	reflux	0
2	PPh_3	dioxane	reflux	74
3	PCy_3	dioxane	reflux	40
4	DPPE	dioxane	reflux	<5
5	DPPF	dioxane	reflux	<5
6	TFP	dioxane	reflux	18
7	PPh_3	dioxane	reflux	52[c]
8	PPh_3	DMF	120 °C	0
9	PPh_3	toluene	reflux	61
10	PPh_3	DMSO	120 °C	9
11	PPh_3	THF	reflux	31
12	PPh_3	dioxane	reflux	55[d]

[a] Conditions: **1a** (0.5 mmol), aniline (**2a**; 0.75 mmol), $Pd(OAc)_2$ (5 mol-%), ligand (10 mol-%), base (1.0 mmol), solvent (1 mL), nitrogen. [b] Isolated yield. [c] Cs_2CO_3 was used as base. [d] $[Pd_2(dba)_3]$ was used as catalyst.

With the above optimized reaction conditions, we explored the substrate scope of the reaction. Interestingly, attempts to expand the generality and applicability of the reaction proved successful, thus providing a functional handle for further manipulation. As illustrated in Table 2, **1a** readily reacted with functionalized arylamines bearing *ortho*, *meta*, and *para* substituents on the aryl ring to give the corresponding products **3b**–**3l** in moderate-to-good yields (Table 2, entries 2–12). Arylamines containing electron-donating groups (Table 2, entries 2–4, and 11) gave higher yields than those with electron-withdrawing groups (Table 2, entries 5–10). However, this reaction was not limited to simple aromatic amines; the pyridine-containing substrate **2m** also afforded **3m** in good yield (Table 2, entry 13). Note also that aliphatic amines such as benzylamine (**2n**) and cyclopropylamine (**2o**) gave products **3n** and **3o**, respectively, in moderate yields (Table 2, entries 14 and 15).

Next, chalcones **1b**–**1m** were investigated in the reaction of aniline (**2a**) under the optimized conditions. Different functional groups R^1 and R^2 of chalcone **1** were all tolerated (Table 3, entries 1–14). Note that the products **3y** and

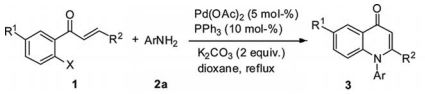
Table 2. Palladium-catalyzed reactions of **1a** with primary amines.[a]

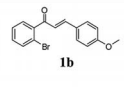
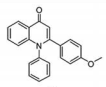
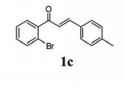
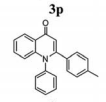
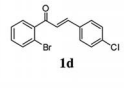
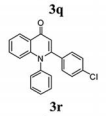
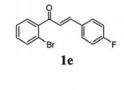
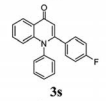
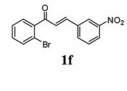
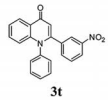
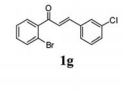
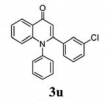
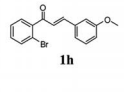
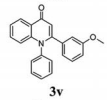
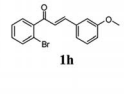
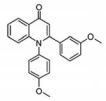
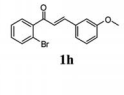
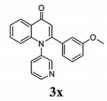
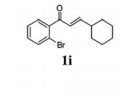
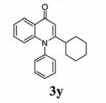
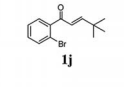
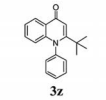
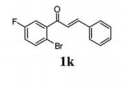
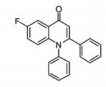
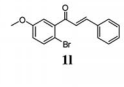
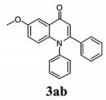
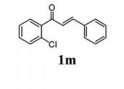
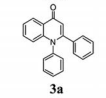


Entry	RNH_2	Product	Yield [%][b]	Time [h]
1	**2a**	**3a**	74	4
2	**2b**	**3b**	87	4
3	**2c**	**3c**	79	5
4	**2d**	**3d**	82	24
5	**2e**	**3e**	76	4
6	**2f**	**3f**	66	5
7	**2g**	**3g**	65	5
8	**2h**	**3h**	54	48
9	**2i**	**3i**	61	24
10	**2j**	**3j**	60	4
11	**2k**	**3k**	79	12
12	**2l**	**3l**	33	12
13	**2m**	**3m**	77	48
14	**2n**	**3n**	52	10
15	**2o**	**3o**	45	8

[a] All reactions were performed under N_2 on a 0.5 mmol scale with arylamines (1.5 equiv.), $Pd(OAc)_2$ (5 mol-%), PPh_3 (10 mol-%), and K_2CO_3 (2.0 equiv.) in anhydrous 1,4-dioxane (1 mL) at reflux. [b] Isolated yield.

Table 3. Palladium-catalyzed reactions of chalcones **1** with aniline.[a]



Entry	Substrate	Product	Yield [%][b]	Time [h]
1	 1b	 3p	78	7
2	 1c	 3q	86	6
3	 1d	 3r	89	4
4	 1e	 3s	77	5
5	 1f	 3t	65	5
6	 1g	 3u	72	4
7	 1h	 3v	61	4
8	 1h	 3w	75	3 [c]
9	 1h	 3x	73	7 [d]
10	 1i	 3y	53	5
11	 1j	 3z	65	5
12	 1k	 3aa	51	7
13	 1l	 3ab	41	2
14	 1m	 3a	15	5 [e]

[a] All reactions were performed under N_2 on a 0.5 mmol scale with arylamines (1.5 equiv.), $Pd(OAc)_2$ (5 mol-%), PPh_3 (10 mol-%), and K_2CO_3 (2.0 equiv.) in anhydrous 1,4-dioxane (1 mL) at reflux. [b] Isolated yield. [c] *p*-Methoxyaniline was used as a primary amine. [d] *m*-Aminopyridine was used as a primary amine. [e] The reaction temperature was 140 °C.

3z were generated in moderate yields when R^2 is an aliphatic group (Table 3, entries 10 and 11). However, due to the low oxidative addition reactivity of the C–Cl bond, chloro-substituted substrate **1m** gave product **3a** in low yield upon raised temperature (Table 3, entry 14).

A plausible reaction mechanism for this one-pot synthesis of 1,2-disubstituted 4-quinolones is outlined in Scheme 2 (Paths A and B).[20b–20d] In Path A, oxidative addition of **1a** to the Pd^0 catalyst leads to palladium complex **A**. The C=C bond in **A** can be activated through coordination to the Pd^{II} and attacked by aniline to form intermediate **D**. Note, intermediate **C** was not formed from complex **A** under these conditions. Path B involves the Michael addition of aniline to **1a** and oxidative addition, and then intermediate **D** is formed by elimination of HBr. Both pathways proceed via intermediate **D**, followed by reductive elimination of Pd^0 to yield **E**. Intermediate **E** leads to **3a** by catalytic dehydrogenation of Pd^0, which is the key step.[21]

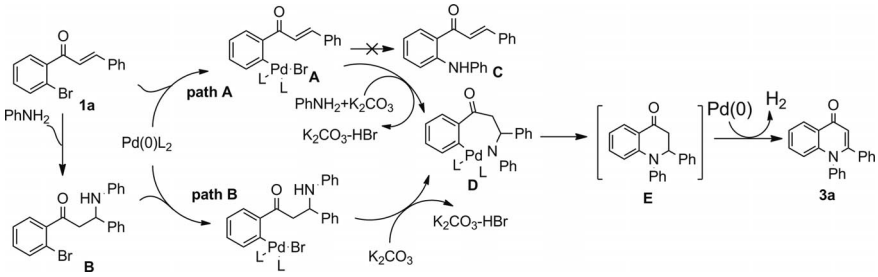
Conclusions

We have developed an efficient palladium-catalyzed tandem amination protocol for the synthesis of 1,2-disubstituted 4-quinolones from easily accessible chalcones and primary amines in which the catalyst palladium plays a dual role, namely in the Buchwald–Hartwig coupling and catalytic dehydrogenation. This approach provides one of the simplest methods for the synthesis of this class of valuable compounds, and a wide range of multisubstituted 4-quinolones could be generated accordingly in the construction of a chemical library.

Experimental Section

General: Anhydrous dioxane was obtained by distillation over metallic sodium. Other solvents and reagents were used as received. TLC was performed on silica HSGF254 plates. Melting points were determined with a digital melting-point apparatus. ^1H, ^{13}C, and ^{19}F NMR spectra were obtained from a solution in $CDCl_3$ or DMSO with TMS as internal standard using a 400/101/377 MHz ($^1H/^{13}C/^{19}F$) or 300/75 MHz ($^1H/^{13}C$) spectrometer. Chemical shifts (δ) are given in ppm and J in Hz. IR spectra were recorded in KBr tablets and wavenumbers are given in cm^{-1}. HRMS were recorded by using an electrospray ionization (ESI) mass spectrometer.

1-(2-Bromophenyl)-3-phenylprop-2-en-1-one (1a): Chalcones **1** were prepared following the known procedure.[22] Benzaldehyde (1.061 g, 10 mmol) and NaOH (2.5 M, 80 mL) were added to a solution of *o*-bromoacetophenone (1.991 g, 10 mmol) in EtOH (200 mL) at room temp. The mixture was stirred for 3 h, neutralized with diluted HCl, and extracted with EtOAc. The organic layer was dried (Na_2SO_4) and the solvents evaporated. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:50) to give **1a** as a yellow oil (2.613 g, 91%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.8 Hz, 1 H), 7.60–7.49 (m, 2 H), 7.48–7.28 (m, 7 H), 7.10 (d, J = 16.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.6, 146.6, 141.0, 134.3, 133.3, 131.3, 130.9, 129.1, 128.9, 128.5, 127.3, 126.0, 119.4 ppm.



Scheme 2. Plausible mechanism for the synthesis of **3a** from **1a**.

1-(2-Bromophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (1b): Yellow solid (2.411 g, 76%); m.p. 88–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.8 Hz, 1 H), 7.51 (d, J = 8.6 Hz, 2 H), 7.44–7.28 (m, 4 H), 6.94 (dd, J = 15.3, 12.5 Hz, 3 H), 3.84 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.8, 161.9, 146.7, 141.3, 133.3, 131.1, 130.4, 129.0, 127.2, 127.0, 123.9, 119.4, 114.4, 55.4 ppm.

1-(2-Bromophenyl)-3-(*p*-tolyl)prop-2-en-1-one (1c): Yellow solid (2.560 g, 85%); m.p. 75–77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.6 Hz, 1 H), 7.51–7.29 (m, 6 H), 7.20 (d, J = 7.7 Hz, 2 H), 7.05 (d, J = 16.1 Hz, 1 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.8, 146.9, 141.6, 141.2, 133.4, 131.6, 131.2, 129.7, 129.1, 128.6, 127.3, 125.2, 119.5, 21.5 ppm.

1-(2-Bromophenyl)-3-(4-chlorophenyl)prop-2-en-1-one (1d): White solid (1.897 g, 59%); m.p. 101–103 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.3 Hz, 1 H), 7.55–7.29 (m, 8 H), 7.07 (d, J = 16.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.3, 144.8, 140.9, 136.8, 133.4, 132.9, 131.5, 129.7, 129.3, 129.2, 127.4, 126.5, 119.5 ppm.

1-(2-Bromophenyl)-3-(4-fluorophenyl)prop-2-en-1-one (1e): Yellow oil (0.915 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.5 Hz, 1 H), 7.54 (s, 2 H), 7.37 (dd, J = 17.8, 8.5 Hz, 4 H), 7.06 (dd, J = 22.5, 12.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.4, 165.9, 162.5, 145.1, 141.0, 133.4, 131.4, 130.5, 130.4, 129.1, 127.3, 125.8, 119.4, 116.3, 116.0 ppm.

1-(2-Bromophenyl)-3-(3-nitrophenyl)prop-2-en-1-one (1f): Yellow solid (1.561 g, 47%); m.p. 142–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.40 (s, 1 H), 8.26 (d, J = 8.1 Hz, 1 H), 7.89 (d, J = 7.5 Hz, 1 H), 7.74–7.57 (m, 2 H), 7.56–7.33 (m, 4 H), 7.23 (d, J = 16.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.7, 148.6, 142.7, 140.5, 136.2, 133.9, 133.5, 131.9, 130.0, 129.3, 128.4, 127.5, 124.9, 122.8, 119.5 ppm.

1-(2-Bromophenyl)-3-(3-chlorophenyl)prop-2-en-1-one (1g): Yellow solid (1.351 g, 42%); m.p. 54–56 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.7 Hz, 1 H), 7.53 (s, 1 H), 7.47–7.28 (m, 7 H), 7.09 (d, J = 16.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.2, 144.5, 140.8, 136.2, 135.0, 133.4, 131.6, 130.6, 130.2, 129.2, 128.2, 127.4, 127.2, 126.6, 119.4 ppm.

1-(2-Bromophenyl)-3-(3-methoxyphenyl)prop-2-en-1-one (1h): Yellow oil (2.506 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.7 Hz, 1 H), 7.47–7.27 (m, 5 H), 7.11 (dd, J = 17.5, 9.0 Hz, 3 H), 6.96 (d, J = 7.7 Hz, 1 H), 3.82 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.6, 159.9, 146.5, 141.0, 135.7, 133.4, 131.3, 129.9, 129.1, 127.3, 126.3, 121.2, 119.4, 116.8, 113.2, 55.3 ppm.

1-(2-Bromophenyl)-3-cyclohexylprop-2-en-1-one (1i): Yellow oil (1.085 g, 37%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, J = 7.8 Hz, 1 H), 7.42–7.28 (m, 3 H), 6.62 (dd, J = 15.9, 6.6 Hz, 1 H), 6.39 (d, J = 16.0 Hz, 1 H), 2.30–2.14 (m, 1 H), 1.85–1.63 (m, 5 H), 1.34–1.13 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.7, 157.9, 141.1, 133.3, 131.0, 129.0, 127.7, 127.1, 119.3, 40.9, 31.5, 25.9, 25.6 ppm.

1-(2-Bromophenyl)-4,4-dimethylpent-2-en-1-one (1j): Yellow oil (2.458 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, J = 7.8 Hz, 1 H), 7.40–7.25 (m, 3 H), 6.67 (d, J = 16.1 Hz, 1 H), 6.36 (d, J = 16.1 Hz, 1 H), 1.10 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.6, 162.1, 141.0, 133.2, 131.0, 128.9, 127.1, 125.3, 119.2, 34.1, 28.4 ppm.

1-(2-Bromo-5-fluorophenyl)-3-phenylprop-2-en-1-one (1k): Yellow solid (1.343 g, 44%); m.p. 73–75 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65–7.49 (m, 3 H), 7.44 (d, J = 14.4 Hz, 4 H), 7.11 (ddd, J = 16.1, 8.7, 4.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.2, 163.3, 160.0, 147.2, 142.6, 142.6, 135.0, 134.9, 134.1, 131.1, 129.0, 128.7, 125.5, 118.8, 118.5, 116.5, 116.2, 113.7, 113.6 ppm.

1-(2-Bromo-5-methoxyphenyl)-3-phenylprop-2-en-1-one (1l): Yellow solid (2.601 g, 82%); m.p. 110–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (dd, J = 6.5, 3.0 Hz, 2 H), 7.50 (d, J = 8.8 Hz, 1 H), 7.45 (d, J = 16.1 Hz, 1 H), 7.40 (dd, J = 5.0, 1.8 Hz, 3 H), 7.08 (d, J = 16.1 Hz, 1 H), 6.95 (d, J = 3.0 Hz, 1 H), 6.88 (dd, J = 8.8, 3.1 Hz, 1 H), 3.81 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.4, 158.9, 146.6, 141.9, 134.4, 134.2, 130.9, 129.0, 128.6, 126.0, 117.6, 114.3, 109.7, 55.6 ppm.

1-(2-Chlorophenyl)-3-phenylprop-2-en-1-one (1m): Yellow oil (1.966 g, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63–7.31 (m, 10 H), 7.15 (d, J = 16.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.7, 146.2, 139.0, 134.3, 131.3, 131.2, 130.8, 130.2, 129.2, 128.9, 128.5, 126.8, 126.2 ppm.

General Procedure for the Synthesis of 1,2-Diphenylquinolin-4(1*H*)-one (3a): Reactions were carried out under nitrogen. Aniline (**2a**; 0.75 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (13.1 mg, 0.05 mmol), and K_2CO_3 (138.2 mg, 1.0 mmol) were added to an oven-dried, nitrogen-purged flask containing **1a** (0.5 mmol) in anhydrous 1,4-dioxane (1 mL). The reaction mixture was stirred under reflux and monitored by TLC. Upon completion, the reaction mixture was filtered and the residue was purified by column chromatography on silica gel by using ethyl acetate/petroleum ether (1:3) as eluent to afford pure product **3a** as a yellow solid (109 mg, 74%); m.p. 281–283 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, J = 7.9 Hz, 1 H), 7.47 (t, J = 7.2 Hz, 1 H), 7.41–7.30 (m, 4 H), 7.20–7.15 (m, 7 H), 6.91 (d, J = 8.6 Hz, 1 H), 6.45 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.9, 154.0, 142.5, 139.0, 135.6, 131.8, 129.9, 129.5, 129.1, 128.9, 128.5, 127.8, 126.2, 126.0, 123.7, 118.0, 112.4 ppm. IR (KBr): $\tilde{\nu}$ = 1629, 1595, 1492, 1478, 1458, 1405, 1313, 1136, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{16}NO$ [M + H]$^+$ 298.1226; found 298.1235.

2-Phenyl-1-(*p*-tolyl)quinolin-4(1*H*)-one (3b): Yellow solid (135 mg, 87%); m.p. 210–212 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.51 (d, J = 7.9 Hz, 1 H), 7.46 (t, J = 7.0 Hz, 1 H), 7.36 (t, J = 7.4 Hz, 1 H), 7.24–7.10 (m, 7 H), 7.02 (d, J = 8.1 Hz, 2 H), 6.92 (d, J = 8.5 Hz, 1 H), 6.43 (s, 1 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.9, 154.1, 142.7, 138.9, 136.4, 135.7, 131.8, 130.1, 129.6, 129.1, 128.5, 127.8, 126.2, 126.1, 123.7, 118.1, 112.5, 21.1 ppm. IR (KBr): $\tilde{\nu}$ = 3051, 1628, 1599, 1514, 1464, 1415, 1319, 835, 748, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO$ [M + H]$^+$ 312.1383; found 312.1395.

1-(4-Methoxyphenyl)-2-phenylquinolin-4(1*H*)-one (3c): Yellow solid (129 mg, 79%); m.p. 193–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, J = 7.8 Hz, 1 H), 7.47 (t, J = 7.2 Hz, 1 H), 7.37 (t, J = 7.3 Hz, 1 H), 7.25–7.11 (m, 5 H), 7.06 (d, J = 8.7 Hz, 2 H), 6.93 (d, J = 8.5 Hz, 1 H), 6.84 (d, J = 8.7 Hz, 2 H), 6.43 (s, 1 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.9, 159.4, 154.4, 142.9, 135.7, 131.8, 131.7, 130.8, 129.1, 128.5, 127.9, 126.1, 126.0, 123.7, 118.1, 114.6, 112.4, 55.4 ppm. IR (KBr): $\tilde{\nu}$ = 1626, 1599, 1508, 1462, 1406, 1252, 1028, 839, 758, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO_2$ [M + H]$^+$ 328.1332; found 328.1333.

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-phenylquinolin-4(1*H*)-one (3d): White solid (140 mg, 82%); m.p. 188–190 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (d, J = 8.0 Hz, 1 H), 7.50 (t, J = 7.7 Hz, 1 H), 7.38 (t, J = 7.4 Hz, 1 H), 7.31–7.15 (m, 5 H), 7.00 (d, J = 8.6 Hz, 1 H), 6.74 (d, J = 8.5 Hz, 1 H), 6.62 (d, J = 5.7 Hz, 2 H), 6.43 (s, 1 H), 6.00 (d, J = 12.0 Hz, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.9, 154.3, 148.5, 147.8, 142.9, 135.7, 132.7, 131.9, 129.1, 128.7, 128.0, 126.3, 123.8, 123.7, 118.0, 112.6, 110.5, 108.4, 102.0 ppm. IR (KBr): $\tilde{\nu}$ = 1630, 1600, 1497, 1481, 1466, 1420, 1234, 1038, 937, 748, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{16}NO_3$ [M + H]$^+$ 342.1125; found 342.1140.

1-(4-Chlorophenyl)-2-phenylquinolin-4(1*H*)-one (3e): White solid (126 mg, 76%); m.p. 204–206 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (dd, J = 8.0, 1.4 Hz, 1 H), 7.49 (ddd, J = 8.7, 7.1, 1.7 Hz, 1 H), 7.42–7.30 (m, 3 H), 7.26–7.19 (m, 3 H), 7.18–7.07 (m, 4 H), 6.87 (d, J = 8.5 Hz, 1 H), 6.44 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.8, 153.7, 142.3, 137.6, 135.3, 134.9, 132.0, 131.3, 129.8, 129.0, 128.8, 128.0, 126.3, 126.0, 123.9, 117.7, 112.7 ppm. IR (KBr): $\tilde{\nu}$ = 3030, 1618, 1599, 1493, 1463, 1408, 1317, 835, 762, 702 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}ClNO$ [M + H]$^+$ 332.0837; found 332.0850.

1-(4-Fluorophenyl)-2-phenylquinolin-4(1*H*)-one (3f): White solid (104 mg, 66%); m.p. 220–222 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.48 (dd, J = 8.0, 1.3 Hz, 1 H), 7.54–7.42 (m, 1 H), 7.37 (t, J = 7.1 Hz, 1 H), 7.26–7.11 (m, 7 H), 7.05 (t, J = 8.4 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 1 H), 6.41 (s, 1 H) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = –111.0 (s, Ar-F) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.8, 163.3, 160.8 (d, $^1J_{C\text{-}F}$ = 186.75 Hz), 153.9, 142.5, 135.4, 135.0 (d, $^4J_{C\text{-}F}$ = 2.25 Hz), 132.0, 131.8, 131.7 (d, $^3J_{C\text{-}F}$ = 6.75 Hz), 129.1, 128.7, 128.0, 126.3, 126.0, 123.8, 117.7, 116.7, 116.5 (d, $^2J_{C\text{-}F}$ = 17.25 Hz), 112.6 ppm. IR (KBr): $\tilde{\nu}$ = 1622, 1595, 1506, 1480, 1464, 1406, 1317, 1211, 1153, 838, 775, 708 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}FNO$ [M + H]$^+$ 316.1132; found 316.1142.

1-(4-Acetylphenyl)-2-phenylquinolin-4(1*H*)-one (3g): Yellow solid (110 mg, 65%); m.p. 218–220 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (dd, J = 8.0, 1.5 Hz, 1 H), 7.95 (d, J = 8.5 Hz, 2 H), 7.47 (ddd, J = 8.7, 7.1, 1.7 Hz, 1 H), 7.38 (t, J = 7.1 Hz, 1 H), 7.29 (d, J = 8.5 Hz, 2 H), 7.25–7.12 (m, 5 H), 6.85 (d, J = 8.5 Hz, 1 H), 6.44 (s, 1 H), 2.59 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.6, 177.8, 153.4, 143.2, 142.1, 137.0, 135.2, 132.1, 130.4, 129.5, 129.0, 128.9, 128.1, 126.4, 126.0, 124.0, 117.6, 112.8, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 1683, 1627, 1597, 1463, 1402, 1262, 762, 706 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{18}NO_2$ [M + H]$^+$ 340.1332; found 340.1342.

1-(4-Nitrophenyl)-2-phenylquinolin-4(1*H*)-one (3h): Yellow solid (93 mg, 54%); m.p. 265–267 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (d, J = 7.2 Hz, 1 H), 8.23 (d, J = 8.1 Hz, 2 H), 7.50 (t, J = 7.3 Hz, 1 H), 7.40 (t, J = 7.3 Hz, 3 H), 7.26–7.19 (m, 3 H), 7.16 (d, J = 6.6 Hz, 2 H), 6.81 (d, J = 8.5 Hz, 1 H), 6.45 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.7, 153.0, 147.4, 144.8, 141.8, 134.8, 132.3, 131.4, 129.2, 129.0, 128.3, 126.6, 125.9, 124.9, 124.2, 117.2, 113.0 ppm. IR (KBr): $\tilde{\nu}$ = 1630, 1601, 1592, 1518, 1493, 1402, 1344, 1314, 756, 706 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}N_2O_3$ [M + H]$^+$ 343.1077; found 343.1090.

3-[4-Oxo-2-phenylquinolin-1(4*H*)-yl]benzonitrile (3i): Yellow solid (98 mg, 61%); m.p. 262–264 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.46 (d, J = 7.9 Hz, 1 H), 7.64 (d, J = 7.3 Hz, 1 H), 7.57–7.44 (m, 4 H), 7.37 (t, J = 7.5 Hz, 1 H), 7.27–7.07 (m, 5 H), 6.78 (d, J = 8.5 Hz, 1 H), 6.39 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.6, 153.2, 141.9, 140.0, 134.8, 133.5, 132.5, 132.2, 130.6, 129.0, 128.2, 126.4, 125.8, 124.1, 117.2, 117.0, 113.8, 112.8 ppm. IR (KBr): $\tilde{\nu}$ = 3040, 2230, 1629, 1601, 1481, 1466, 1416, 1319, 748, 706 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{15}N_2O$ [M + H]$^+$ 323.1179; found 323.1195.

2-Phenyl-1-[3-(phenylsulfonyl)phenyl]quinolin-4(1*H*)-one (3j): White solid (131 mg, 60%); m.p. 336–338 °C. ^{1}H NMR (400 MHz, DMSO): δ = 8.29 (d, J = 7.5 Hz, 1 H), 8.17 (s, 1 H), 7.89 (d, J = 8.3 Hz, 1 H), 7.84 (d, J = 7.4 Hz, 2 H), 7.76 (t, J = 6.4 Hz, 2 H), 7.71–7.58 (m, 4 H), 7.45 (t, J = 7.4 Hz, 1 H), 7.19 (d, J = 7.3 Hz, 2 H), 7.05 (t, J = 7.5 Hz, 1 H), 6.95 (t, J = 7.5 Hz, 2 H), 6.79 (d, J = 8.5 Hz, 1 H), 6.13 (s, 1 H) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 176.1, 153.5, 142.2, 141.9, 140.4, 139.8, 135.4, 134.9, 133.8, 132.4, 131.1, 129.7, 129.6, 128.9, 128.3, 127.6, 127.3, 125.4, 125.3, 123.7, 117.8, 111.2 ppm. IR (KBr): $\tilde{\nu}$ = 3059, 1626, 1601, 1408, 1320, 1304, 1155, 758, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{20}NO_3S$ [M + H]$^+$ 438.1158; found 438.1175.

2-Phenyl-1-(*m*-tolyl)quinolin-4(1*H*)-one (3k): Yellow solid (122 mg, 79%); m.p. 222–224 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.51 (d, J = 7.1 Hz, 1 H), 7.52–7.41 (m, 1 H), 7.36 (t, J = 7.4 Hz, 1 H), 7.25–7.09 (m, 7 H), 6.95 (t, J = 7.0 Hz, 3 H), 6.43 (s, 1 H), 2.28 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 153.9, 142.5, 139.6, 138.8, 135.6, 131.7, 130.3, 129.5, 129.2, 129.0, 128.5, 127.7, 126.8, 126.0, 125.9, 123.6, 118.1, 112.3, 21.0 ppm. IR (KBr): $\tilde{\nu}$ = 1629, 1595, 1478, 1460, 1406, 1307, 1136, 761, 708 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO$ [M + H]$^+$ 312.1383; found 312.1398.

2-Phenyl-1-(*o*-tolyl)quinolin-4(1*H*)-one (3l): Red solid (51 mg, 33%); m.p. 255–257 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59–8.47 (m, 1 H), 7.52–7.45 (m, 1 H), 7.40 (t, J = 7.3 Hz, 1 H), 7.29–7.16 (m, 9 H), 6.77 (d, J = 8.5 Hz, 1 H), 6.49 (s, 1 H), 1.93 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.7, 154.0, 141.8, 137.9, 136.6, 135.3, 132.2, 131.5, 130.5, 129.5, 128.8, 127.8, 127.0, 126.4, 126.1, 123.9, 117.6, 112.7, 17.5 ppm. IR (KBr): $\tilde{\nu}$ = 1627, 1595, 1477, 1460, 1406, 1310, 1138, 775, 760, 727, 702 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO$ [M + H]$^+$ 312.1383; found 312.1397.

2-Phenyl-1-(pyridin-3-yl)quinolin-4(1*H*)-one (3m): White solid (115 mg, 77%); m.p. 200–202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (dd, J = 4.7, 1.0 Hz, 1 H), 8.53–8.44 (m, 2 H), 7.57–7.46 (m, 2 H), 7.43–7.31 (m, 2 H), 7.25–7.19 (m, 3 H), 7.16 (dd, J = 6.5, 3.0 Hz, 2 H), 6.82 (d, J = 8.6 Hz, 1 H), 6.45 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.8, 153.7, 150.9, 149.8, 142.4, 137.4, 136.0, 134.9, 132.3, 129.1, 129.0, 128.3, 126.6, 126.0, 124.2, 124.1, 117.4, 112.8 ppm. IR (KBr): $\tilde{\nu}$ = 3042, 1630, 1601, 1574, 1482, 1414, 1319, 762, 748, 704 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{15}N_2O$ [M + H]$^+$ 299.1179; found 299.1184.

1-Benzyl-2-phenylquinolin-4(1*H*)-one (3n): Yellow solid (80 mg, 52%); m.p. 146–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, J = 7.3 Hz, 1 H), 7.55–7.48 (m, 1 H), 7.45–7.39 (m, 1 H), 7.39–7.31 (m, 6 H), 7.31–7.21 (m, 3 H), 6.98 (d, J = 7.2 Hz, 2 H), 6.34 (s, 1 H), 5.27 (s, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.6, 155.1, 141.2, 136.4, 135.7, 132.2, 129.6, 129.0, 128.6, 128.1, 127.6, 127.2, 126.8, 125.5, 123.7, 117.2, 113.1, 52.1 ppm. IR (KBr): $\tilde{\nu}$ = 1615, 1596, 1556, 1486, 1413, 1269, 766, 735, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO$ [M + H]$^+$ 312.1383; found 312.1393.

1-Cyclopropyl-2-phenylquinolin-4(1*H*)-one (3o): Yellow solid (59 mg, 45%); m.p. 168–170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43 (d, J = 7.9 Hz, 1 H), 7.96 (d, J = 8.6 Hz, 1 H), 7.69 (t, J = 7.6 Hz, 1 H), 7.53–7.47 (m, 5 H), 7.39 (t, J = 7.4 Hz, 1 H), 6.31 (s, 1 H), 3.42–3.27 (m, 1 H), 0.94 (d, J = 6.3 Hz, 2 H), 0.56 (d, J = 2.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1, 155.4, 143.0, 136.8, 131.6, 129.1, 128.4, 128.3, 126.6, 126.3, 123.5, 117.8, 113.2, 32.3, 12.9 ppm. IR (KBr): $\tilde{\nu}$ = 1613, 1594, 1555, 1486, 1462, 1416, 777, 765, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{16}NO$ [M + H]$^+$ 262.1226; found 262.1237.

2-(4-Methoxyphenyl)-1-phenylquinolin-4(1*H*)-one (3p): White solid (128 mg, 78%); m.p. 205–207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.51 (d, J = 7.7 Hz, 1 H), 7.52–7.29 (m, 5 H), 7.16 (d, J = 6.5 Hz, 2 H), 7.08 (d, J = 7.9 Hz, 2 H), 6.90 (d, J = 8.4 Hz, 1 H), 6.69 (d, J = 7.9 Hz, 2 H), 6.43 (s, 1 H), 3.74 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.9, 159.5, 153.9, 142.6, 139.2, 131.8, 130.5, 129.9, 129.6, 128.8, 128.0, 126.1, 125.9, 123.7, 118.0, 113.3, 112.6, 55.1 ppm. IR (KBr): $\tilde{\nu}$ = 3046, 1624, 1601, 1510, 1481, 1402, 1250, 1186, 1024, 839, 776, 760 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO_2$ [M + H]$^+$ 328.1332; found 328.1333.

1-Phenyl-2-(*p*-tolyl)quinolin-4(1*H*)-one (3q): Yellow solid (133 mg, 86%); m.p. 289–291 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, J = 7.2 Hz, 1 H), 7.52–7.31 (m, 5 H), 7.16 (s, 2 H), 7.01 (d, J = 14.1 Hz, 4 H), 6.90 (d, J = 8.2 Hz, 1 H), 6.43 (s, 1 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 154.1, 142.5, 139.2, 138.5, 132.7, 131.7, 129.9, 129.5, 129.0, 128.8, 128.5, 126.1, 126.0, 123.6, 118.0, 112.5, 21.1 ppm. IR (KBr): $\tilde{\nu}$ = 1630, 1595, 1508, 1493, 1478, 1458, 1403, 1313, 1136, 762, 706 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO$ [M + H]$^+$ 312.1383; found 312.1397.

2-(4-Chlorophenyl)-1-phenylquinolin-4(1*H*)-one (3r): White solid (148 mg, 89%); m.p. 232–234 °C. ^{1}H NMR (300 MHz, DMSO): δ = 8.27 (d, J = 7.0 Hz, 1 H), 7.59 (t, J = 7.1 Hz, 1 H), 7.51–7.24 (m, 10 H), 6.83 (d, J = 8.5 Hz, 1 H), 6.16 (s, 1 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.2, 152.9, 142.4, 138.8, 134.5, 133.5, 132.4, 131.2, 130.2, 129.8, 129.3, 127.9, 125.6, 125.4, 123.9, 118.3, 111.4 ppm. IR (KBr): $\tilde{\nu}$ = 3054, 1629, 1608, 1593, 1495, 1480, 1414, 1316, 754, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}ClNO$ [M + H]$^+$ 332.0837; found 332.0853.

2-(4-Fluorophenyl)-1-phenylquinolin-4(1*H*)-one (3s): White solid (121 mg, 77%); m.p. 225–227 °C. ^{1}H NMR (300 MHz, DMSO): δ = 8.28 (d, J = 6.8 Hz, 1 H), 7.60 (t, J = 7.0 Hz, 1 H), 7.42 (s, 8 H), 7.08 (t, J = 8.7 Hz, 2 H), 6.83 (d, J = 8.4 Hz, 1 H), 6.16 (s, 1 H) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = –111.8 (s, Ar-F) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.2, 163.5, 160.2 (d, $^1J_{C\text{-}F}$ = 247.5 Hz), 153.1, 142.4, 138.9, 132.4, 132.1 (d, $^4J_{C\text{-}F}$ = 3 Hz), 131.7, 131.6 (d, $^3J_{C\text{-}F}$ = 8.25 Hz), 130.2, 129.7, 129.2, 125.6, 125.4, 123.8, 118.3, 115.0, 114.7 (d, $^2J_{C\text{-}F}$ = 21 Hz), 111.5 ppm. IR (KBr): $\tilde{\nu}$ = 3045, 1628, 1595, 1511, 1494, 1483, 1420, 1319, 847, 747 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}FNO$ [M + H]$^+$ 316.1132; found 316.1147.

2-(3-Nitrophenyl)-1-phenylquinolin-4(1*H*)-one (3t): Yellow solid (111 mg, 65%); m.p. 279–281 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (d, J = 8.0 Hz, 1 H), 8.08 (d, J = 8.5 Hz, 1 H), 8.04 (s, 1 H), 7.55 (d, J = 7.4 Hz, 1 H), 7.49 (t, J = 7.5 Hz, 1 H), 7.45–7.29 (m, 5 H), 7.19 (d, J = 7.2 Hz, 2 H), 6.90 (d, J = 8.5 Hz, 1 H), 6.41 (s, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.7, 151.0, 147.4, 142.5, 138.5, 137.1, 134.9, 132.3, 130.0, 129.8, 129.5, 129.2, 126.3, 126.0, 124.2, 123.5, 118.0, 112.7 ppm. IR (KBr): $\tilde{\nu}$ = 3056, 3045, 1628, 1604, 1595, 1526, 1493, 1346, 841, 816, 744, 706 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}N_2O_3$ [M + H]$^+$ 343.1077; found 343.1080.

2-(3-Chlorophenyl)-1-phenylquinolin-4(1*H*)-one (3u): White solid (119 mg, 72%); m.p. 272–274 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, J = 7.9 Hz, 1 H), 7.50–7.35 (m, 5 H), 7.17–7.08 (m, 5 H), 7.05 (d, J = 7.5 Hz, 1 H), 6.91 (d, J = 8.5 Hz, 1 H), 6.41 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 152.2, 142.5, 138.8, 137.2, 133.8, 132.0, 129.9, 129.7, 129.2, 128.8, 127.3, 126.3, 126.0, 123.9, 118.0, 112.5 ppm. IR (KBr): $\tilde{\nu}$ = 3042, 1627, 1595, 1495, 1470, 1423, 1404, 1317, 800, 748 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}ClNO$ [M + H]$^+$ 332.0837; found 332.0848.

2-(3-Methoxyphenyl)-1-phenylquinolin-4(1*H*)-one (3v): White solid (100 mg, 61%); m.p. 217–219 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50 (dd, J = 7.7, 1.2 Hz, 1 H), 7.53–7.31 (m, 5 H), 7.18 (d, J = 4.2 Hz, 2 H), 7.09 (t, J = 7.9 Hz, 1 H), 6.92 (d, J = 8.5 Hz, 1 H), 6.80–6.63 (m, 3 H), 6.45 (s, 1 H), 3.68 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 158.8, 153.7, 142.5, 139.1, 136.7, 131.8, 129.9, 129.5, 128.9, 126.2, 126.0, 123.7, 121.7, 118.0, 114.7, 114.4, 112.4, 55.2 ppm. IR (KBr): $\tilde{\nu}$ = 3051, 3037, 1627, 1602, 1595, 1578, 1480, 1291, 1057, 748, 712 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO_2$ [M + H]$^+$ 328.1332; found 328.1340.

2-(3-Methoxyphenyl)-1-(4-methoxyphenyl)quinolin-4(1*H*)-one (3w): Yellow solid (134 mg, 75%); m.p. 178–180 °C. ^{1}H NMR (300 MHz, DMSO): δ = 8.26 (d, J = 7.8 Hz, 1 H), 7.59 (t, J = 6.9 Hz, 1 H), 7.42 (d, J = 7.1 Hz, 1 H), 7.34 (d, J = 8.3 Hz, 2 H), 7.17 (t, J = 7.7 Hz, 1 H), 7.05–6.73 (m, 6 H), 6.15 (s, 1 H), 3.74 (s, 3 H), 3.67 (s, 3 H) ppm. ^{13}C NMR (75 MHz, DMSO): δ = 176.2, 159.1, 158.4, 154.3, 142.9, 137.0, 132.3, 131.6, 131.3, 129.1, 125.7, 125.3, 123.7, 121.5, 118.4, 114.9, 114.6, 114.5, 111.2, 55.5, 55.2 ppm. IR (KBr): $\tilde{\nu}$ = 3056, 1626, 1597, 1508, 1463, 1407, 1250, 1032, 841, 760 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{20}NO_3$ [M + H]$^+$ 358.1438; found 358.1455.

2-(3-Methoxyphenyl)-1-(pyridin-3-yl)quinolin-4(1*H*)-one (3x): White solid (120 mg, 73%); m.p. 213–215 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.60 (s, 1 H), 8.49 (d, J = 7.8 Hz, 2 H), 7.58–7.48 (m, 2 H), 7.39–7.29 (m, 2 H), 7.12 (t, J = 6.8 Hz, 1 H), 6.84–6.71 (m, 4 H), 6.46 (s, 1 H), 3.70 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 159.1, 153.5, 150.8, 149.8, 142.3, 137.4, 136.0, 132.3, 129.4, 126.5, 126.0, 124.1, 124.0, 121.6, 117.4, 114.8, 114.7, 112.7, 55.2 ppm. IR (KBr): $\tilde{\nu}$ = 1630, 1597, 1481, 1464, 1423, 1406, 1319, 1292, 1267, 1039, 1028, 750 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{17}N_2O_2$ [M + H]$^+$ 329.1285; found 329.1292.

2-Cyclohexyl-1-phenylquinolin-4(1*H*)-one (3y): Yellow solid (81 mg, 53%); m.p. 240–242 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, J = 7.7 Hz, 1 H), 7.62 (s, 3 H), 7.37 (t, J = 7.6 Hz, 1 H), 7.29 (d, J = 11.1 Hz, 3 H), 6.61 (d, J = 8.5 Hz, 1 H), 6.40 (s, 1 H), 2.11 (t, J = 11.5 Hz, 1 H), 1.80 (d, J = 12.6 Hz, 2 H), 1.70 (d, J = 12.9 Hz, 2 H), 1.59 (d, J = 12.9 Hz, 1 H), 1.42 (q, J = 12.4 Hz, 2 H), 1.17 (q, J = 12.9 Hz, 1 H), 0.94 (q, J = 12.6 Hz, 2 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.2, 159.6, 142.6, 138.6, 131.3, 130.3, 129.7, 129.0, 125.8, 125.7, 123.3, 118.2, 108.2, 41.1, 33.0, 26.2, 25.5 ppm. IR (KBr): $\tilde{\nu}$ = 2940, 2847, 1626, 1601, 1489, 1465, 1423, 1303, 1136, 844, 781, 760, 710 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}NO$ [M + H]$^+$ 304.1696; found 304.1688.

2-*tert*-Butyl-1-phenylquinolin-4(1*H*)-one (3z): Yellow solid (91 mg, 65%); m.p. 219–221 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (d, J = 7.6 Hz, 1 H), 7.56 (d, J = 6.4 Hz, 3 H), 7.40–7.18 (m, 4 H), 6.66 (s, 1 H), 6.40 (d, J = 8.7 Hz, 1 H), 1.16 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.8, 161.3, 144.8, 140.4, 131.6, 131.4, 129.8, 129.3, 125.4, 125.0, 123.2, 118.3, 110.1, 37.5, 31.7 ppm. IR (KBr): $\tilde{\nu}$ = 1623, 1560, 1571, 1488, 1464, 1391, 1315, 847, 764, 715 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{14}FNO$ [M + H]$^+$ 316.1132; found 316.1143. HRMS (ESI): calcd. for $C_{19}H_{20}NO$ [M + H]$^+$ 278.1539; found 278.1532.

6-Fluoro-1,2-diphenylquinolin-4(1*H*)-one (3aa): Yellow solid (81 mg, 51%); m.p. 269–271 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (dd, J = 8.9, 3.0 Hz, 1 H), 7.40–7.32 (m, 3 H), 7.21–7.14 (m, 8 H), 6.90 (dd, J = 9.4, 4.3 Hz, 1 H), 6.40 (s, 1 H) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = –117.8 (s, Ar-F) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9, 160.8, 157.5 (d, $^1J_{C\text{-}F}$ = 244.5 Hz), 154.0, 139.0 (d, $^6J_{C\text{-}F}$ = 4.5 Hz), 135.4, 129.8, 129.6 (d, $^4J_{C\text{-}F}$ = 14.25 Hz), 129.1, 128.6, 127.9, 127.5, 127.4 (d, $^5J_{C\text{-}F}$ = 6.75 Hz), 120.4, 120.1 (d, $^3J_{C\text{-}F}$ = 18.75 Hz), 111.8, 110.8, 110.5 (d, $^2J_{C\text{-}F}$ = 22.5 Hz), 104.7 ppm. IR (KBr): $\tilde{\nu}$ = 3046, 1616, 1595, 1496, 1478, 1395, 1310, 1182, 839, 779, 704 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}FNO$ [M + H]$^+$ 316.1132; found 316.1143.

6-Methoxy-1,2-diphenylquinolin-4(1*H*)-one (3ab): White solid (67 mg, 41%); m.p. 244–246 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 3.0 Hz, 1 H), 7.39–7.29 (m, 3 H), 7.21–7.12 (m, 7 H), 7.09 (dd, J = 9.3, 3.1 Hz, 1 H), 6.85 (d, J = 9.3 Hz, 1 H), 6.42 (s, 1 H), 3.94 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.2, 156.3, 153.0, 139.3, 137.3, 135.7, 130.0, 129.5, 129.2, 128.9, 128.5, 127.8, 127.2, 122.5, 119.8, 111.6, 105.2, 55.8 ppm. IR (KBr): $\tilde{\nu}$ = 1607, 1593, 1491, 1479, 1309, 1032, 779, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO_2$ [M + H]$^+$ 328.1332; found 328.1340.

Supporting Information (see footnote on the first page of this article): ^{1}H, ^{13}C, and ^{19}F NMR spectra.

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[1] F. C. Santos, P. Abreu, H. C. Castro, I. C. P. P. Paixão, C. C. Cirne-Santos, V. Giongo, J. E. Barbosa, B. R. Simonetti, V. Garrido, D. C. Bou-Habib, D. O. Silva, P. N. Batalha, J. R. Temerozo, T. M. Souza, C. M. Nogueira, A. C. Cunha, C. R. Rodrigues, V. F. Ferreira, M. C. B. V. Souza, *Bioorg. Med. Chem.* **2009**, *17*, 5476–5481.

[2] a) M. Hadjeri, E.-L. Peiller, C. Beney, N. Deka, A. Lawson, C. Dumontet, A. Boumendjel, *J. Med. Chem.* **2004**, *47*, 4964–4970; b) Y.-Y. Lai, L.-J. Huang, K.-H. Lee, Z. Xiao, K. F. Bastow, T. Yamoric, S.-C. Kuo, *Bioorg. Med. Chem.* **2005**, *13*, 265–275.

[3] D. Edmont, R. Rocher, C. Plisson, J. Chenault, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1831–1834.

[4] a) T. P. T. Cushnie, J. Lamb, *Phytomedicine* **2006**, *13*, 187–191; b) X. Ma, W. Zhou, R. Brun, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 986–989; c) A. A. Wube, F. Bucar, C. Hochfellner, M. Blunder, R. Bauer, A. Hüfner, *Eur. J. Med. Chem.* **2011**, *46*, 2091–2101.

[5] a) Y. Xia, Z.-Y. Yang, P. Xia, K. F. Bastow, Y. Nakanishi, P. Nampoothiri, E. Hamel, A. Brossia, K.-H. Lee, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2891–2893; b) S. Nakamura, M. Kozuka, K. F. Bastow, H. Tokuda, H. Nishino, M. Suzuki, J. Tatsuzaki, S. L. M. Natschke, S.-C. Kuo, K.-H. Lee, *Bioorg. Med. Chem.* **2005**, *13*, 4396–4401; c) Q.-D. You, Z.-Y. Li, C.-H. Huang, Q. Yang, X.-J. Wang, Q.-L. Guo, X.-G. Chen, X.-G. He, T.-K. Li, J.-W. Chern, *J. Med. Chem.* **2009**, *52*, 5649–5661.

[6] a) M. Sato, T. Motomura, H. Aramaki, T. Matsuda, M. Yamashita, Y. Ito, H. Kawakami, Y. Matsuzaki, W. Watanabe, K. Yamataka, S. Ikeda, E. Kodama, M. Matsuoka, H. Shinkai, *J. Med. Chem.* **2006**, *49*, 1506–1508; b) R. D. Santo, R. Costi, A. Roux, M. Artico, A. Lavecchia, L. Marinelli, E. Novellino, L. Palmisano, M. Andreotti, R. Amici, C. M. Galluzzo, L. Nencioni, A. T. Palamara, Y. Pommier, C. Marchand, *J. Med. Chem.* **2006**, *49*, 1939–1945; c) R. Dayam, L. Q. Al-Mawsawi, Z. Zawahir, M. Witvrouw, Z. Debyser, N. Neamati, *J. Med. Chem.* **2008**, *51*, 1136–1144; d) M. Sato, H. Kawakami, T. Motomura, H. Aramaki, T. Matsuda, M. Yamashita, Y. Ito, Y. Matsuzaki, K. Yamataka, S. Ikeda, H. Shinkai, *J. Med. Chem.* **2009**, *52*, 4869–4882; e) Q.-Q. He, S.-X. Gu, J. Liu, H.-Q. Wua, X. Zhang, L.-M. Yang, Y.-T. Zheng, F.-E. Chen, *Bioorg. Med. Chem.* **2011**, *19*, 5039–5045.

[7] F. V. Yang, W. D. Shipe, J. L. Bunda, M. B. Nolt, D. D. Wisnoski, Z. Zhao, J. C. Barrow, W. J. Ray, L. Mab, M. Wittmann, M. A. Seager, K. A. Koeplinger, G. D. Hartman, C. W. Lindsley, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 531–536.

[8] a) D. Ding, X. Li, X. Wang, Y. Du, J. Shen, *Tetrahedron Lett.* **2006**, *47*, 6997–6999; b) C. P. Jones, K. W. Anderson, S. L. Buchwald, *J. Org. Chem.* **2007**, *72*, 7968–7973; c) J. Huang, Y. Chen, A. O. King, M. Dilmeghani, R. D. Larsen, M. M. Faul, *Org. Lett.* **2008**, *10*, 2609–2612.

[9] a) P. Hradil, M. Grepl, J. Hlaváč, M. Soural, M. Maloň, V. Bertolasi, *J. Org. Chem.* **2006**, *71*, 819–822; b) E. Stern, G. G. Muccioli, B. Bosier, L. Hamtiaux, R. Millet, J. H. Poupaert, J. P. Hénichart, P. Depreux, J.-F. Goossens, D. M. Lambert, *J. Med. Chem.* **2007**, *50*, 5471–5484.

[10] Y. Yoshino, T. Kurahashi, S. Matsubara, *J. Am. Chem. Soc.* **2009**, *131*, 7494–7495.

[11] a) W. M. Abdou, A. A. Kamel, *Synth. Commun.* **2007**, *37*, 3945–3960; b) A. A. Kamel, W. M. Abdou, *Synlett* **2007**, 1269–1273.

[12] S.-C. Kuo, H.-Z. Lee, J.-P. Juang, Y.-T. Lin, T.-S. Wu, J.-J. Chang, D. Lednicer, K. D. Paull, C. M. Lin, E. Hamel, K.-H. Lee, *J. Med. Chem.* **1993**, *36*, 1146–1156.

[13] P. Hradil, J. Hlavac, K. Lemr, *J. Heterocycl. Chem.* **1999**, *36*, 141–144.

[14] T. R. Ward, B. J. Turunen, T. Haack, B. Neuenswander, W. Shadrick, G. Georg, *Tetrahedron Lett.* **2009**, *50*, 6494–6497.

[15] a) R. Weiss, M. Bess, S. M. Huber, F. W. Heinemann, *J. Am. Chem. Soc.* **2008**, *130*, 4610–4617; b) M. M. Škugor, V. Štimac, I. Palej, D. Lugarić, H. Č. Paljetak, D. Filić, M. Modrić, I. Dilović, D. Gembarovski, S. Mutak, V. E. Haber, D. J. Holmes, Z. Ivezić-Schoenfeld, S. Alihodžić, *Bioorg. Med. Chem.* **2010**, *18*, 6547–6558; c) O. Tabarrini, S. Massari, D. Daelemans, F. Meschini, G. Manfroni, L. Bottega, B. Gatto, M. Palumbo, C. Pannecouque, V. Cecchetti, *ChemMedChem* **2010**, *5*, 1880–1892.

[16] a) J. A. Donnelly, D. F. Farrell, *J. Org. Chem.* **1990**, *55*, 1757–1761; b) A. L. Tökés, G. Litkei, L. Szilágyi, *Synth. Commun.* **1992**, *22*, 2433–2445; c) C. Praveen, K. Parthasarathy, P. T. Perumal, *Synlett* **2010**, *11*, 1635–1640.

[17] D. Zewge, C. Chen, C. Deer, P. G. Dormer, D. L. Hughes, *J. Org. Chem.* **2007**, *72*, 4276–4279.

[18] a) V. N. Kalinin, M. V. Sbostakovsky, A. B. Ponomaryov, *Tetrahedron Lett.* **1992**, *33*, 373–376; b) S. Torii, H. Okumoto, L. H. Xu, M. Sadakane, M. V. Shostakovsky, A. B. Ponomaryov, V. N. Kalinin, *Tetrahedron* **1993**, *49*, 6773–6784; c) N. Haddad, J. Tan, V. Farina, *J. Org. Chem.* **2006**, *71*, 5031–5034; d) M. Genelot, A. Bendjeriou, V. Dufaud, L. Djakovitch, *Appl. Catal. A* **2009**, *369*, 125–132; e) M. Genelot, V. Dufaud, L. Djakovitch, *Tetrahedron* **2011**, *67*, 976–981.

[19] Q.-L. Liu, Q.-L. Li, X.-D. Fei, Y.-M. Zhu, *ACS Comb. Sci.* **2011**, *13*, 19–23.
[20] a) R. Bernini, S. Cacchi, G. Fabrizi, A. Sferrazza, *Synthesis* **2009**, 1209–1219; b) T. Zhao, B. Xu, *Org. Lett.* **2010**, *12*, 212–215; c) Z. Zheng, H. Alper, *Org. Lett.* **2008**, *10*, 829–832; d) J. F. Hartwig, *Angew. Chem.* **1998**, *110*, 2154; *Angew. Chem. Int. Ed.* **1998**, *37*, 2046–2067.
[21] a) Y. Shvo, A. H. I. Arisha, *J. Org. Chem.* **1998**, *63*, 5640–5642; b) T. Ohmura, A. Kijima, M. Suginome, *Org. Lett.* **2011**, *13*, 1238–1241.
[22] İ. Karamana, H. Gezegen, M. B. Gürdere, A. Dingil, M. Ceylan, *Chem. Biodiversity* **2010**, *7*, 400–408.

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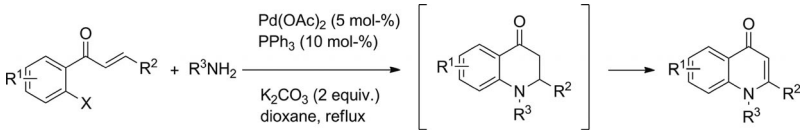
Catalytic Dehydrogenation



The Buchwald–Hartwig coupling/Michael addition sequence has been successfully used for the synthesis of 1,2-disubstituted 4-quinolones starting from chalcones and primary amines using $Pd(OAc)_2/PPh_3/K_2CO_3$ as the catalyst system. The intermediates formed underwent catalytic dehydrogenation to give the products in good yields. The methodology has a broad scope and is applicable to library synthesis.

Keywords: Palladium / Cyclization / Michael addition / Dehydrogenation / Heterocycles

