Synthesis of *N*-Alkyl-Substituted 4-Quinolones via Tandem Alkenyl and Aryl C–N Bond Formation

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Abstract: *N*-Alkyl-substituted 4-quinolones are present as the key structural motif in many marketed drugs. An efficient one-step tandem amination approach was developed to afford *N*-alkyl-substituted 4-quinolones in high yields from easily accessible *o*-chloroaryl acetylenic ketones and functionalized alkyl amines. The approach complements and extends our previous work. Compared with other reported methods, the current method provides a very simple and convenient route.

Key words: alkynes, amination, cyclization, nitrogen heterocycles, domino reactions

The 4-quinolone structural motif appears as the core structure of several biologically active molecules and in various natural products.[1] Such compounds have a wide variety of activities and have been developed as antibiotics,[2] anticancer agents,[3] and various inhibitors.[4] Typical commercially available compounds with these characteristics are drugs such as Ciprofloxacin, Norfloxacin, and Moxifloxacin, which are used for the treatment of bacterial infections with high efficiency (Figure 1). Such characteristics have made the molecules significant synthetic targets and the development of efficient synthetic methods for this structural moiety continues to be of tremendous interest.[5] In this context, some elegant one-pot reactions for the construction of the 4-quinolone scaffold, using 2′-aminoacetophenone derivatives,[6] 2′-bromoacetophenones,[7] *o*-halophenones,[8] 2-iodoanilines,[9] as well as the reactions of isatoic anhydrides with aryl ketones[10a] or alkynes,[10b] have been intensely studied.

Recently, we developed an efficient palladium-catalysed tandem amination protocol for the direct synthesis of *N*-aryl 4-quinolones (Scheme 1).[11a] However, when alkyl amine was employed as the nitrogen unit, the yield was significantly decreased (e.g., 42% yield for *n*-butylamine),[11a] which was unfortunate because such *N*-alkyl-substituted 4-quinolone moieties are privileged structures in many clinically used drugs (Figure 1). To address this problem, new synthetic strategies needed to be developed that would enable the facile synthesis of *N*-alkyl-substituted 4-quinolones. Previously, we focused our study on the effective construction of nitrogen-containing molecules via tandem C–N/C–N coupling reactions,[11a] C–N/Suzuki–Miyaura coupling,[11b] C–N/Sonogashira coupling,[11c] and C–N/C–O coupling.[11d] Herein, we describe a successful extension of this concept, whereby a sequential double C–N bond was formed to give *N*-alkyl-substituted 4-quinolones in high yields from readily available substrates (Scheme 1). To our knowledge, this tandem reaction represents the first efficient example of a one-pot synthesis of *N*-alkyl-substituted 4-quinolones from *o*-chloroaryl acetylenic ketones and functionalized alkyl amines through a double C–N bond-forming process.

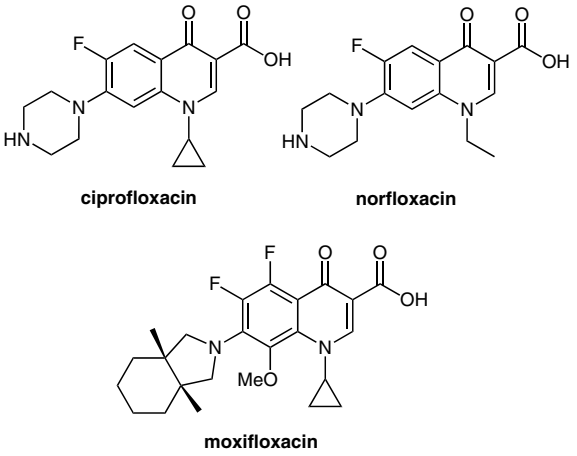

Figure 1 Some bioactive compounds containing the 4-quinolone moiety

We started our investigation by reacting **1a** with *n*-butylamine in the presence of Cs_2CO_3 in dimethyl sulfoxide (DMSO) at 140 °C. To our delight, the reaction gave 1-butyl-4-quinolone **3aa** in 86% yield (Table 1, entry 1). Amongst the other bases tested, K_2CO_3 (entry 2) and K_3PO_4 (entry 6) proved to be the most efficient, whereas Na_2CO_3, Li_2CO_3 and $NaHCO_3$ gave diminished yields (entries 3–5). The reaction using K_3PO_4 as base in DMSO was slightly faster than with K_2CO_3. Screening a range of solvents revealed that DMSO was the best solvent for this reaction (entry 6). Using *N*-methyl-2-pyrrolidinone (NMP), toluene, dioxane, or 2-methyl-2-butanol (*t*-AmOH)

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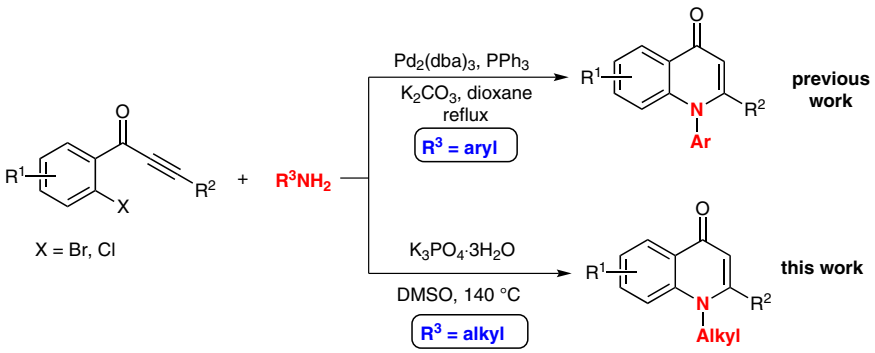


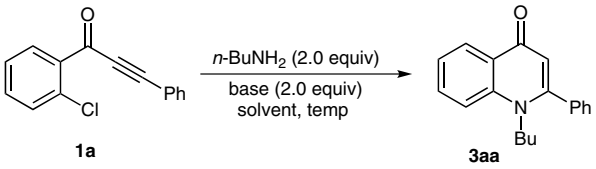
Scheme 1 A tandem amination strategy for the synthesis of N-functionalized 4-quinolones from alkynones and alkyl amines

as solvent gave much lower yields (entries 7–10), whereas $MeNO_2$ failed to give any product (entry 11). In the presence of a twofold excess of *n*-butylamine, the amount of K_3PO_4 could be reduced to 1.5 equivalents and the reaction afforded **3aa** in 95% yield (entry 12). Lower temperatures retarded the reaction and gave **3aa** in 80% yield (entry 13). The presence of tetrabutylammonium bromide (TBAB) as a phase-transfer catalyst allowed a reduction in the reaction temperature, but afforded **3aa** in 85% yield with longer reaction time (entry 14).

The optimised reaction conditions, using K_3PO_4 in DMSO (Table 1, entry 12), were very broadly applicable and tolerated a wide variety of substitution patterns and functionalities, as shown in Table 2. Alkyl amines with a range of aliphatic chain lengths reacted with **1a** smoothly to afford the corresponding quinolones **3aa**–**ac** in excellent yields (Table 2, entries 1–3). Isopropylamine also performed well and gave **3ad** in 70% yield (entry 4), perhaps due to its low nucleophilicity.[12] Cyclic amines with various ring sizes reacted with comparable efficiency (entries 5 and 6), although the steric hindrance associated with the cyclohexyl group resulted in a lower reactivity in this reaction (entry 6). Substrate **2g** with an active hydroxy functionality could be readily incorporated and produced **3ag** selectively in 94% yield (entry 7), without the formation of any by-products through intermolecular nucleophilic attack of the oxygen. Benzylamine and allylamine performed better in this reaction, and generated **3ah** and **3ai** in 96 and 72% yield, respectively (entries 8 and 9). The latter product was characterised as the more thermodynamically stable product in which the carbon–carbon double bond of the allyl group had migrated (entry 9). However, the less basic aniline gave only a trace amount of product under the optimised conditions, and **3aj** could be afforded in only 8% yield using more reactive bromo-substituted substrate **1k**; no major intermediate formed during the reactions (entry 10). In the latter case, we found that improved yields could be achieved by using a modified stepwise one-pot procedure for aniline (Scheme 2); the reason may be due to the easy formation of the Michael addition product in the absence of base. Extension of the primary amine series to include benzamide or tosylamide, failed to give the corresponding quinolone derivatives, and the reaction generated a complex mixture.

To further explore the generality and scope of this approach, a variety of ynones **1b**–**k**[11a] were investigated. As shown in Table 3, this method was compatible with different types of ynones substituted with aryl, alkyl, and TMS groups (Table 3, entries 1–11). Substrates containing either electron-donating (entries 1 and 2) or electron-

Table 1 Optimization of the Synthesis of **3aa**[a]



Entry	Solvent	Base	Temp (°C)	Time (h)	Yield (%)[b]
1	Cs_2CO_3	DMSO	140	4.5	86
2	K_2CO_3	DMSO	140	4.5	93
3	Na_2CO_3	DMSO	140	2	35
4	Li_2CO_3	DMSO	140	2	<5
5	$NaHCO_3$	DMSO	140	2	34
6	$K_3PO_4·3H_2O$	DMSO	140	2	93
7	$K_3PO_4·3H_2O$	NMP	140	2	22
8	$K_3PO_4·3H_2O$	toluene	reflux	2	<5
9	$K_3PO_4·3H_2O$	dioxane	reflux	2	<5
10	$K_3PO_4·3H_2O$	*t*-AmOH	120	2	<5
11	$K_3PO_4·3H_2O$	$MeNO_2$	reflux	2	0
12	$K_3PO_4·3H_2O$	DMSO	140	2	95[c]
13	$K_3PO_4·3H_2O$	DMSO	120	11	80[c]
14	$K_3PO_4·3H_2O$	DMSO	120	6	85[c,d]

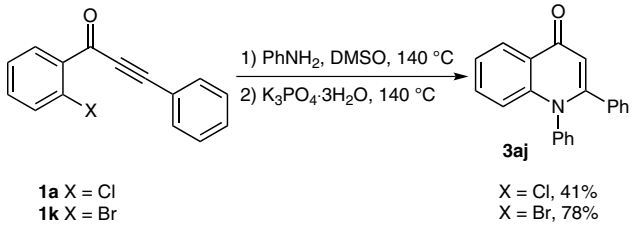
[a] Reaction conditions: **1a** (0.2 mmol), *n*-butylamine (**2a**; 0.4 mmol), base (0.4 mmol), solvent (1.5 mL), reaction performed in a capped tube.
[b] Isolated yield.
[c] Conditions A: **1a** (0.2 mmol), *n*-butylamine (**2a**; 0.6 mmol), $K_3PO_4·3H_2O$ (0.3 mmol), DMSO (1.5 mL), 140 °C.
[d] TBAB (1.0 equiv) was used.

Table 2 Reaction of **1a** with Primary Amines[a]

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

Entry	Amine (R)		Product (R)		Time (h)	Yield (%)[b]
1	**2a**	*n*-Bu	**3aa**	*n*-Bu	2	95
2	**2b**	$Me(CH_2)_7$	**3ab**	$Me(CH_2)_7$	4	94
3	**2c**	$Me(CH_2)_{11}$	**3ac**	$Me(CH_2)_{11}$	4	89
4	**2d**	*i*-Pr	**3ad**	*i*-Pr	10.5	70
5	**2d**	*c*-Pr	**3ae**	*c*-Pr	2	88
6	**2f**	*c*-Hex	**3af**	*c*-Hex	10	53
7	**2g**	$HOCH_2CH_2$	**3ag**	$HOCH_2CH_2$	2	94
8	**2h**	Bn	**3ah**	Bn	2	96
9	**2i**	$H_2C{=}CHCH_2$	**3ai**	MeCH=CH	4.5	72[c]
10	**2j**	Ph	**3aj**	Ph	11	trace (8[d])

[a] Reaction conditions (0.5 mmol scale): amine (1.5–3.0 equiv), $K_3PO_4{\cdot}3H_2O$ (1.5 equiv), DMSO (3 mL), 140 °C.
[b] Isolated yield.
[c] Double-bond migration product **3ai** was obtained.
[d] 1-(2-Bromophenyl)-3-phenylpropynone (**1k**) was used.

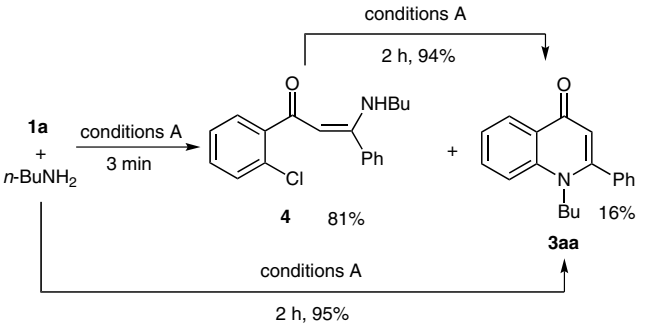


Scheme 2 Stepwise one-pot synthesis of *N*-phenyl-4-quinolone

withdrawing groups (entries 3–7), or bearing *para*- (entries 1–4), *meta*- (entries 5 and 7), or *ortho*- (entry 6) substituents on the aryl ring generally gave the products in excellent yields. Heptyl-substituted ynone **1h** afforded **3ha** in 88% yield, albeit after longer reaction time (entry 8). Dichloro-substituted ynone **1i** afforded the corresponding quinolones **3ia** and **3ie** in excellent yields without competitive reactions occurring on the second chlorine atom (entries 9–10). A tandem double C–N bond formation and desilylation process was observed with trimethylsilyl-substituted substrate **1j** that gave the synthetically useful product **3je** in good yield (entry 11), which proved to be a key intermediate for the direct synthesis of Ciprofloxacin through sequential carboxylation with carbon dioxide[13] and amination reaction with piperazine.[14] It should be noted that the bromo-substituted substrate **1k** afforded a similar result to that obtained with **1a** (cf. Table 3, entry 12 vs. Table 2, entry 1).

The produced quinolones **3** were also very useful synthetic precursors, for example, the corresponding 3-functionalized quinolones could be easily generated using well-documented amination,[15] cyanation,[16] Heck,[17] Sonogashira,[18] and Suzuki–Miyaura reactions[11a,19] from 3-halogenated quinolones, which could be prepared by direct halogenation of our products **3**.[11a,19a]

To investigate the mechanism, the reaction intermediate **4**[20,21] was isolated in 81% yield after running the reaction for three minutes from **1a** and *n*-butylamine (**2a**) under conditions A (Table 1, note c), together with 16% yield of quinolone product **3aa** (Scheme 3).[22] Furthermore, the isolated intermediate **4** could further transform into **3aa** in 94% yield under conditions A (Scheme 3). The two-step reaction could yield **3aa** in approximately 92% overall yield from **1a** and **2a**; a result that is comparable with the one-step yield (95%; Table 2, entry 1). Based on these results, we envisioned that this tandem reaction may predominantly proceed through intermediate **4** to afford the target quinolone **3aa**.

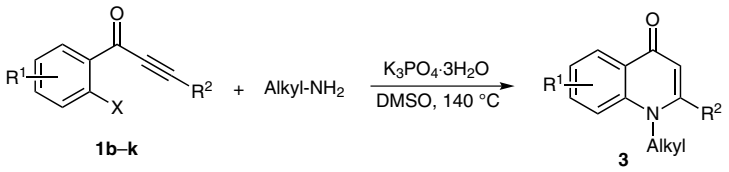


Scheme 3 Plausible mechanism for the synthesis of **3aa** from **1a**

In summary, we have developed an efficient method for the straightforward synthesis of N-functionalized 4-quinolones from easily accessible *o*-chloroaryl acetylenic ketones and alkyl amines that provides a successful extension and complement to our previous work.[11a] A wide range of electronically and structurally varied nitrogen fragments could be introduced through this tandem C–N bond-forming process. Compared with other reported methods, the current approach provides a very simple and convenient route. The produced *N*-alkyl-substituted 4-quinolones are present as the key structural motif in many marketed drugs, and the approach should find applications in medicinal chemistry. Further studies on the application of this method for the construction of bioactive compounds are under investigation in our laboratory and will be reported in due course.

All reagents and solvents were obtained from commercial sources and were purified before use. Melting points were measured with a WRS-1A or a WRS-1B digital melting point apparatus without correction. Infrared spectra were obtained with an AVATAR 370 FTIR spectrometer. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded with a

Table 3 Reaction of Alkynones with Alkylamines[a]



Entry	1	X	R^1	R^2	2	Product	Time (h)	Yield (%)[b]
1	**1b**	Cl	H	4-$MeOC_6H_4$	**2a**	**3ba**	3.5	99
2	**1c**	Cl	H	4-EtC_6H_4	**2a**	**3ca**	6	98
3	**1d**	Cl	H	4-FC_6H_4	**2a**	**3da**	4	98
4	**1e**	Cl	H	4-ClC_6H_4	**2a**	**3ea**	4	80
5	**1f**	Cl	H	3-ClC_6H_4	**2a**	**3fa**	2	96
6	**1g**	Cl	H	2-ClC_6H_4	**2a**	**3ga**	3	90
7	**1f**	Cl	H	3-ClC_6H_4	**2e**	**3fe**	2	91
8	**1h**	Cl	H	*n*-C_5H_{11}	**2a**	**3ha**	20	88
9	**1i**	Cl	H	Ph	**2a**	**3ia**	4.5	94
10	**1i**	Cl	4-Cl	Ph	**2e**	**3ie**	2	94
11	**1j**	Cl	4-Cl-5-F	TMS	**2e**	**3je**[c]	1	61[c]
12	**1k**	Br	H	Ph	**2a**	**3aa**	2	95

[a] Reaction conditions (0.5 mmol scale): amine (1.5–3.0 equiv), $K_3PO_4·3H_2O$ (1.5 equiv), DMSO (3 mL), 140 °C.

[b] Isolated yield.

[c] Desilylation product **3je** (R^2 = H) was obtained.

Bruker AV-500 spectrometer operating at 500, 125 and 470 MHz, respectively, with chemical shift values being reported in ppm relative to the solvent $CDCl_3$ (δ_H = 7.26 ppm; δ_C = 77.16 ppm) or DMSO-d_6 (δ_H = 2.50 ppm; δ_C = 39.52 ppm). Mass spectra were recorded with an Agilent 5975N fitted with an ES ion source unless stated otherwise. Elemental analyses were carried out with an Elementar Vario EL elemental analyzer. Silica gel plates (GF254) were used for thin layer chromatography (TLC) and silica gel H or 300–400 mesh were used for flash column chromatography. Petroleum ether (PE), where used, had a boiling range of 60–90 °C.

1-(2-Chlorophenyl)-3-phenylpropynone (1a)[11a]

To a solution of phenylacetylene (400.0 mg, 3.92 mmol) in freshly dried THF (5 mL) was added slowly *n*-BuLi (2.5 M in hexane, 1.72 mL) at –78 °C under a nitrogen atmosphere and the solution was stirred for 3 min. A solution of 2-chlorobenzaldehyde (460.0 mg, 3.27 mmol) in anhydrous THF (2 mL) was then added slowly while maintaining the temperature at –78 °C, and the reaction was allowed to proceed for 2 h and then warmed to r.t. The reaction mixture was washed with sat. aq NH_4Cl (5 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was dried over Na_2SO_4, and the solvent was evaporated under vacuum to give a crude oil that was used for next step without further purification. To a stirred solution of the crude oil in CH_2Cl_2 (30 mL) was added activated manganese dioxide (2.84 g, commercial sample), and the resulting suspension was stirred at r.t. for 10 h and then filtered through a thin pad of Celite. The residue was purified by column chromatography on silica gel (EtOAc–PE, 1:15) to give **1a**.

Yield: 512.6 mg (65%); yellow oil.

IR (KBr): 2196, 1649, 1587, 1303, 1009, 758, 741 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.10–8.08 (m, 1 H), 7.65–7.64 (m, 2 H), 7.50–7.46 (m, 3 H), 7.43–7.39 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.9, 135.9, 133.6, 133.5, 133.2, 132.7, 131.7, 131.1, 128.8, 126.9, 120.1, 94.1, 88.4.

MS (EI): *m*/*z* (%) = 242 (16) [M^+ (^{37}Cl)], 240 (47) [M^+ (^{35}Cl)], 212 (83), 129 (100).

1-(2-Chlorophenyl)-3-(4-methoxyphenyl)propynone (1b)

Following the same procedure used for **1a** with 1-ethynyl-4-methoxybenzene (571.0 mg, 4.32 mmol), *n*-BuLi (1.6 M in hexane, 3.24 mL), 2-chlorobenzaldehyde (668.0 mg, 4.75 mmol) and activated manganese dioxide (4.79 g, commercial sample) gave **1b**.

Yield: 893.0 mg (76%); yellow solid; mp 56–58 °C.

IR (KBr): 2190, 1644, 1601, 1567, 1510, 1172 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.5 Hz, 1 H), 7.59 (d, *J* = 8.5 Hz, 2 H), 7.47–7.44 (m, 2 H), 7.40–7.38 (m, 1 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 3.84 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.0, 162.0, 136.3, 135.4, 133.5, 133.3, 132.5, 131.6, 126.9, 114.6, 111.9, 95.5, 88.6, 55.6.

MS (EI): *m*/*z* (%) = 272 (26) [M^+ (^{37}Cl)], 270 (69) [M^+ (^{35}Cl)], 242 (42), 159 (100).

Anal. Calcd for $C_{16}H_{11}ClO_2$: C, 70.99; H, 4.10. Found: C, 70.84; H, 3.89.

1-(2-Chlorophenyl)-3-(4-ethylphenyl)propynone (1c)

Following the same procedure used for **1a** with 1-ethynyl-4-ethylbenzene (450.0 mg, 3.45 mmol), *n*-BuLi (1.6 M in hexane, 2.58

mL), 2-chlorobenzaldehyde (533.0 mg, 3.79 mmol) and activated manganese dioxide (4.00 g, commercial sample) gave **1c**.

Yield: 600.0 mg (65%); yellow oil.

IR (film): 2968, 2932, 2873, 2194, 1648, 1604, 1587, 1506, 1465, 1303, 834 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.08–8.06 (m, 1 H), 7.57 (d, *J* = 6.5 Hz, 2 H), 7.48–7.46 (m, 2 H), 7.41–7.25 (m, 1 H), 7.24 (d, *J* = 8.5 Hz, 2 H), 2.69 (q, *J* = 7.5 Hz, 2 H), 1.25 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.0, 148.1, 136.1, 133.6, 133.41, 133.38, 132.6, 131.6, 128.4, 126.9, 117.2, 94.9, 88.4, 29.2, 15.3.

MS (EI): *m*/*z* (%) = 270 (20) [M^+ (^{37}Cl)], 268 (57) [M^+ (^{35}Cl)], 225 (65), 157 (100).

HRMS: *m*/*z* calcd for $C_{17}H_{13}ClO$: 268.0655; found: 268.0652.

1-(2-Chlorophenyl)-3-(4-fluorophenyl)propynone (1d)

To a solution of 1-(2,2-dibromovinyl)-4-fluorobenzene (2.0 g, 7.14 mmol) and benzyltriethylammonium chloride (1.79 g, 7.86 mmol) in CH_2Cl_2 (15 mL), KOH (12.0 g, 0.21 mol) in H_2O (8 mL) was added at 0 °C. The solution was stirred for 1 h at 0 °C, and then extracted with CH_2Cl_2 (2 × 20 mL). The organic layer was dried over Na_2SO_4, filtered through a thin pad of Celite, and concentrated under vacuum to give the crude product. The crude alkynyl bromide was dissolved in THF (5 mL) and *n*-BuLi (1.6 M in hexane, 5.28 mL) was added slowly at –78 °C under a nitrogen atmosphere and the mixture was stirred for 3 min. A solution of the 2-bromobenzaldehyde (1.09 g, 7.73 mmol) in anhydrous THF (2 mL) was then added slowly while maintaining the temperature at –78 °C, and the reaction was allowed to proceed for 2 h and warmed to r.t. The reaction mixture was washed with sat. aq NH_4Cl (5 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under vacuum to give a crude oil that was used for the next step without further purification. To a stirred solution of the crude product in CH_2Cl_2 (30 mL), was added activated manganese dioxide (9.46 g, commercial sample) and the resulting suspension was stirred at r.t. for 1.5 h and then filtered through a thin pad of Celite. The residue was purified by column chromatography on silica gel (EtOAc–PE, 1:15) to give **1d**.

Yield: 1.04 g (57%); yellow solid; mp 78–80 °C.

IR (KBr): 2202, 1637, 1596, 1526, 1503, 1309, 1228, 833, 737 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.06–8.05 (m, 1 H), 7.67–7.63 (m, 2 H), 7.49–7.47 (m, 2 H), 7.42–7.38 (m, 1 H), 7.13–7.08 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8, 164.3 (d, $^1J_{C-F}$ = 252.5 Hz), 135.9, 135.6 (d, $^3J_{C-F}$ = 8.75 Hz), 133.7, 133.6, 132.6, 131.7, 127.1 (d, $^2J_{C-F}$ = 27.5 Hz), 116.5, 116.3 (d, $^4J_{C-F}$ = 3.75 Hz), 93.0, 88.4.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –105.7 (m, Ar-F).

MS (EI): *m*/*z* (%) = 260 (18) [M^+ (^{37}Cl)], 258 (59) [M^+ (^{35}Cl)], 232 (30), 230 (96), 147 (100).

Anal. Calcd for $C_{15}H_8ClFO$: C, 69.65; H, 3.12. Found: C, 69.78; H, 3.18.

3-(4-Chlorophenyl)-1-(2-chlorophenyl)propynone (1e)[23]

To a solution of 1-(2,2-dibromovinyl)-4-chlorobenzene (1.5 g, 5.06 mmol) and benzyltriethylammonium chloride (1.27 g, 5.06 mmol) in CH_2Cl_2 (15 mL), KOH (12.0 g, 0.21 mol) in H_2O (8 mL) was added at 0 °C. The solution was stirred for 1 h at 0 °C and then extracted with CH_2Cl_2 (2 × 20 mL). The organic layer was dried over Na_2SO_4, filtered through a thin pad of Celite, and concentrated under vacuum to give the crude product. The crude alkynyl bromide was dissolved in THF (5 mL) and *n*-BuLi (1.6 M in hexane, 3.8 mL) was added slowly at –78 °C under a nitrogen atmosphere and stirred for 3 min. A solution of 2-chlorobenzaldehyde (0.782 g, 5.57 mmol) in anhydrous THF (2 mL) was then added slowly while maintaining the temperature at –78 °C, and the reaction was allowed to proceed for 2 h and warmed to r.t. The reaction mixture was washed with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under vacuum to give a crude oil that was used for next step without further purification. To a stirred solution of the crude product in CH_2Cl_2 (30 mL), was added activated manganese dioxide (6.60 g, commercial sample), and the resulting suspension was stirred at r.t. for 3.5 h and then filtered through a thin pad of Celite. The residue was purified by column chromatography on silica gel (EtOAc–PE, 1:15) to give **1e**.

Yield: 251.3 mg (28%); yellow solid; mp 83–84 °C.

IR (KBr): 2202, 1635, 1588, 1306, 1012 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.5 Hz, 1 H), 7.57 (d, *J* = 8.5 Hz, 2 H), 7.49–7.46 (m, 2 H), 7.43–7.38 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.7, 137.5, 135.8, 134.4, 133.8, 133.7, 132.6, 131.7, 129.3, 127.0, 118.6, 92.6, 89.1.

MS (EI): *m*/*z* (%) = 278 (5) [M^+ (2 × ^{37}Cl)], 276 (31) [M^+ (^{37}Cl, ^{35}Cl)], 274 (51) [M^+ (2 × ^{35}Cl)], 246 (91), 163 (100).

3-(3-Chlorophenyl)-1-(2-chlorophenyl)propynone (1f)[23]

To a solution of 1-(2,2-dibromovinyl)-3-chlorobenzene (3.0 g, 10.12 mmol) and benzyltriethylammonium chloride (2.54 g, 11.13 mmol) in CH_2Cl_2 (20 mL), KOH (12.0 g, 0.21 mol) in H_2O (8 mL) was added at 0 °C. The solution was stirred for 2 h at 0 °C and then extracted with CH_2Cl_2 (2 × 20 mL). The organic layer were dried over Na_2SO_4, filtered through a thin pad of Celite, and concentrated under vacuum to give the crude product. The crude alkynyl bromide was dissolved in THF (5 mL) and *n*-BuLi (2.2 M in hexane, 5.1 mL) was added slowly at –78 °C under a nitrogen atmosphere and stirred for 3 min. A solution of 2-chlorobenzaldehyde (1.57 g, 11.13 mmol) in anhydrous THF (2 mL) was then added slowly while maintaining the temperature at –78 °C, and the reaction was allowed to proceed for 2 h and warmed to r.t. The reaction mixture was washed with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under vacuum to give a crude oil that was used for the next step without further purification. To a stirred solution of the crude product in CH_2Cl_2 (30 mL) was added activated manganese dioxide (13.20 g, commercial sample), and the resulting suspension was stirred at r.t. for 13 h and then filtered through a thin pad of Celite. The residue was purified by column chromatography on silica gel (EtOAc–PE, 1:15) to give **1f**.

Yield: 1.93 g (69%); yellow solid; mp 77–79 °C.

IR (KBr): 2207, 1639, 1587, 1307, 1016 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.5 Hz, 1 H), 7.60 (s, 1 H), 7.52–7.47 (m, 3 H), 7.44–7.39 (m, 2 H), 7.34 (t, *J* = 7.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.5, 135.6, 134.7, 133.7, 132.7, 132.6, 131.7, 131.3, 131.2, 130.6, 127.0, 121.8, 91.8, 88.8.

MS (EI): *m*/*z* (%) = 278 (8) [M^+ (2 × ^{37}Cl)], 276 (33) [M^+ (^{37}Cl, ^{35}Cl)], 274 (50) [M^+ (2 × ^{35}Cl)], 250 (11), 248 (65), 246 (100), 176 (32), 163 (82).

1,3-Bis(2-chlorophenyl)propynone (1g)[23]

To a solution of 1-chloro-2-(2,2-dibromovinyl)benzene (3.0 g, 10.12 mmol) and benzyltriethylammonium chloride (2.54 g, 11.13 mmol) in CH_2Cl_2 (20 mL), KOH (12.0 g, 0.21 mol) in H_2O (8 mL) was added at 0 °C. The solution was stirred for 2 h at 0 °C and then extracted with CH_2Cl_2 (2 × 20 mL). The organic layer was dried over Na_2SO_4, filtered through a thin pad of Celite, and concentrated under vacuum to give the crude product. The crude alkynyl bromide was dissolved in THF (5 mL) and *n*-BuLi (2.2 M in hexane, 5.1 mL) was added slowly at –78 °C under a nitrogen atmosphere and stirred for 3 min. A solution of 2-bromobenzaldehyde (1.57 g, 11.13

mmol) in anhydrous THF (2 mL) was then added slowly while maintaining the temperature at –78 °C, and the reaction was allowed to proceed for 2 h and warmed to r.t. The reaction mixture was washed with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under vacuum to give a crude oil that was used for next step without further purification. To a stirred solution of the crude product in CH_2Cl_2 (30 mL) was added activated manganese dioxide (13.20 g, commercial sample), and the resulting suspension was stirred at r.t. for 11.5 h and then filtered through a thin pad of Celite. The residue was purified by column chromatography on silica gel (EtOAc–PE, 1:15) to give **1g**.

Yield: 1.48 g (53%); yellow solid; mp 78–80 °C.

IR (KBr): 2200, 1650, 1586, 1205, 1002, 761, 735 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 8.0 Hz, 1 H), 7.67 (d, *J* = 7.5 Hz, 1 H), 7.49–7.39 (m, 5 H), 7.30 (t, *J* = 7.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.5, 137.7, 135.3, 135.1, 133.9, 133.7, 133.5, 132.0, 131.9, 129.8, 127.0, 126.9, 120.4, 92.1, 89.9.

MS (EI): *m*/*z* (%) = 278 (5) [M^+ (2 × ^{37}Cl)], 276 (40) [M^+ (^{37}Cl, ^{35}Cl)], 274 (58) [M^+ (2 × ^{35}Cl)], 250 (14), 248 (70), 246 (100), 163 (80), 111 (46), 83 (41), 71 (42), 57 (65).

1-(2-Chlorophenyl)oct-2-yn-1-one (1h)
Following the same procedure used for **1a** with hept-1-yne (600.0 mg, 6.24 mmol), *n*-BuLi (2.2 M in hexane, 4.67 mL), 2-chlorobenzaldehyde (1.05 g, 7.49 mmol) and activated manganese dioxide (8.15 g, commercial sample) gave **1h**.

Yield: 1.15 g (78%); light-yellow oil.

IR (film): 2957, 2931, 2861, 2209, 1655, 1588, 1566, 1466, 1434, 1284, 1242, 743 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.0–7.99 (m, 1 H), 7.44–7.40 (m, 2 H), 7.38–7.32 (m, 1 H), 2.45 (t, *J* = 7.5 Hz, 2 H), 1.66 (quint, *J* = 7.0 Hz, 2 H), 1.45–1.39 (m, 2 H), 1.37–1.30 (m, 2 H), 0.90 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.1, 136.0, 133.4, 133.2, 132.8, 131.6, 126.8, 98.1, 81.2, 31.2, 27.4, 22.2, 19.4, 14.0.

MS (EI): *m*/*z* (%) = 236 (1) [M^+ (^{37}Cl)], 234 (2) [M^+ (^{35}Cl)], 139 (100).

HRMS: *m*/*z* calcd for $C_{14}H_{15}ClO$: 234.0811; found: 234.0810.

1-(2,4-Dichlorophenyl)-3-phenylpropynone (1i)[24]
Following the same procedure used for **1a** with phenylacetylene (1.6 g, 15.71 mmol), *n*-BuLi (2.2 M in hexane, 7.2 mL), 2,4-dichlorobenzaldehyde (2.5 g, 14.28 mmol) and activated manganese dioxide (18.6 g, commercial sample) gave **1i**.

Yield: 2.60 g (66%); light-yellow solid; mp 88–89 °C.

IR (KBr): 2196, 1639, 1582, 1302, 1203, 1066, 1014 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.5 Hz, 1 H), 7.64 (d, *J* = 7.0 Hz, 2 H), 7.50–7.47 (m, 2 H), 7.43–7.37 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.6, 139.4, 134.7, 134.3, 133.6, 133.2, 131.5, 131.2, 128.9, 127.4, 120.0, 94.6, 88.2.

MS (EI): *m*/*z* (%) = 276 (29) [M^+ (^{37}Cl)], 274 (37) [M^+ (^{35}Cl)], 246 (90), 129 (100).

1-(2,4-Dichloro-5-fluorophenyl)-3-trimethylsilanylpropynone (1j)[25]
A stirred mixture of [$Pd(PPh_3)_2Cl_2$] (65.6 mg, 0.0934 mmol) and CuI (35.6 mg, 0.1868 mmol) in THF (20 mL) was degassed. Et_3N (516.1 mg, 5.1 mmol), 2,4-dichloro-5-fluorobenzoyl chloride (1061.4 mg, 4.67 mmol), and trimethylsilyl acetylene (500.9 mg, 5.1 mmol) were added and the reaction mixture was stirred for 1 h at r.t. The solvents were evaporated under reduced pressure and the residue was purified by chromatography on silica gel (PE) to give **1j**.

Yield: 748.3 mg (55%); yellow solid; mp 38.0–39.5 °C.

IR (KBr): 2155, 1665, 1596, 1568, 1468, 1376, 1255, 1185, 1054, 849 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 9.0 Hz, 1 H), 7.53 (d, *J* = 6.5 Hz, 1 H), 0.30 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.8, 156.4 (d, $^1J_{C-F}$ = 250.0 Hz), 134.6 (d, $^3J_{C-F}$ = 6.0 Hz), 133.2, 129.2 (d, $^4J_{C-F}$ = 3.75 Hz), 126.7 (d, $^2J_{C-F}$ = 18.75 Hz), 120.2 (d, $^2J_{C-F}$ = 23.75 Hz), 103.1, 101.3, –0.92.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –115.8 (m, Ar-F).

MS (EI): *m*/*z* (%) = 292 (4) [M^+ (2 × ^{37}Cl)], 290 (21) [M^+ (^{37}Cl, ^{35}Cl)], 288 (32) [M^+ (2 × ^{35}Cl)], 273 (100).

HRMS: *m*/*z* calcd for $C_{12}H_{11}Cl_2FOSi$: 287.9940; found: 287.9944.

1-(2-Bromophenyl)-3-phenylpropynone (1k)[11a]
To a solution of phenylacetylene (500.0 mg, 4.90 mmol) in freshly dried THF (5 mL) was added slowly *n*-BuLi (2.5 M in hexane, 2.15 mL) at –78 °C under a nitrogen atmosphere and the mixture was stirred for 3 min. A solution of 2-bromobenzaldehyde (824 mg, 4.45 mmol) in anhydrous THF (2 mL) was then added slowly while maintaining the temperature at –78 °C, and the reaction was allowed to proceed for 2 h and warmed to r.t. The reaction mixture was washed with sat. aq NH_4Cl (5 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na_2SO_4, and the solvent was evaporated under vacuum to give a crude oil that was used for the next step without further purification. To a stirred solution of the crude oil in CH_2Cl_2 (30 mL) was added activated manganese dioxide (3.87 g, commercial sample). The resulting suspension was stirred at r.t. for 7 h and then filtered through a thin pad of Celite. The residue was purified by column chromatography on silica gel (EtOAc–PE, 1:15) to give **1k**.

Yield: 781.0 mg (62%); yellow oil.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.07 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.68 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.63 (dd, *J* = 8.5, 1.5 Hz, 2 H), 7.49–7.35 (m, 5 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.6, 137.5, 135.0, 133.5, 133.2, 132.8, 131.1, 128.8, 127.5, 121.3, 120.0, 94.3, 88.0.

MS (ESI): *m*/*z* (%) = 286 (100) [M^+ (^{81}Br)], 284 (93) [M^+ (^{79}Br)].

1-Butyl-2-phenyl-1*H*-quinolin-4-one (3aa)[11a]
To an oven-dried, capped tube containing **1a** (120.4 mg, 0.5 mmol) and $K_3PO_4{\cdot}3H_2O$ (199.7 mg, 0.75 mmol) in DMSO (3.0 mL), butan-1-amine (109.5 mg, 1.5 mmol) was added. The reaction mixture was stirred at 140 °C for 2 h and monitored by TLC. Upon completion, the reaction mixture was washed with H_2O (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phase was washed with brine and dried over Na_2SO_4. The solid was filtered off through a thin pad of Celite, and the filtrate was evaporated under vacuum to give the crude product that was purified by column chromatography on silica gel (EtOAc–PE, 1:1) to give **3aa**.

Yield: 131.8 mg (95%); yellow solid; mp 74–76 °C.

IR (KBr): 1629, 1594, 1482, 1414, 1174, 762 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.51 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.70–7.66 (m, 1 H), 7.53 (d, *J* = 8.5 Hz, 1 H), 7.50–7.48 (m, 3 H), 7.41–7.37 (m, 3 H), 6.23 (s, 1 H), 4.0 (t, *J* = 7.5 Hz, 2 H), 1.64 (quint, *J* = 7.5 Hz, 2 H), 1.18–1.10 (m, 2 H), 0.74 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.5, 154.7, 140.7, 136.1, 132.3, 129.5, 128.8, 128.4, 127.4, 127.1, 123.6, 116.4, 112.9, 48.0, 30.8, 19.8, 13.5.

MS (EI): *m*/*z* (%) = 277 (14) [M^+], 149 (100).

Octyl-2-phenyl-1*H*-quinolin-4-one (3ab)
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), octyl-1-amine (96.9 mg, 0.75 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4 h gave **3ab**.

Yield: 156.7 mg (94%); white solid; mp 73–75 °C.

IR (KBr): 2954, 2930, 2850, 1620, 1595, 761 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.53 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.72–7.68 (m, 1 H), 7.56–7.50 (m, 4 H), 7.42–7.39 (m, 3 H), 6.25 (s, 1 H), 4.01 (t, *J* = 7.5 Hz, 2 H), 1.67 (quint, *J* = 7.0 Hz, 2 H), 1.26–1.12 (m, 10 H), 0.86 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.4, 154.6, 140.7, 136.2, 132.2, 129.5, 128.8, 128.4, 127.5, 127.1, 123.6, 116.3, 112.9, 48.2, 31.7, 29.0, 28.8, 28.7, 26.5, 22.6, 14.2.

MS (EI): *m*/*z* (%) = 333 (34) [M^+], 234 (100).

Anal. Calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20. Found: C, 82.68; H, 7.94; N, 4.14.

Dodecyl-2-phenyl-1*H*-quinolin-4-one (3ac)
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), dodecyl-1-amine (139.0 mg, 0.75 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4 h gave **3ac**.

Yield: 156.7 mg (89%); white solid; mp 83–84 °C.

IR (KBr): 2952, 2917, 2850, 1620, 1595, 761 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.51 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.70–7.66 (m, 1 H), 7.53–7.46 (m, 4 H), 7.40–7.37 (m, 3 H), 6.22 (s, 1 H), 3.98 (t, *J* = 7.5 Hz, 2 H), 1.66–1.64 (m, 2 H), 1.29–1.09 (m, 18 H), 0.86 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.4, 154.6, 140.7, 136.2, 132.3, 129.5, 128.8, 128.4, 127.5, 127.1, 123.6, 116.3, 113.0, 48.2, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 28.9, 28.7, 26.5, 22.8, 14.2.

MS (EI): *m*/*z* (%) = 388 (78) [M^+ – Me], 234 (100).

Anal. Calcd for $C_{27}H_{35}NO$: C, 83.24; H, 9.06; N, 3.60. Found: C, 83.22; H, 8.87; N, 3.49.

Isopropyl-2-phenyl-1*H*-quinolin-4-one (3ad)[26]
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), propan-2-amine (88.7 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 10.5 h gave **3ad**.

Yield: 91.9 mg (70%); white solid; mp 217–218 °C.

IR (KBr): 2975, 2936, 2878, 1628, 1596 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.52 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.82 (d, *J* = 8.5 Hz, 1 H), 7.64–7.61 (m, 1 H), 7.48–7.47 (m, 3 H), 7.39–7.35 (m, 3 H), 6.18 (s, 1 H), 4.71–4.62 (m, 1 H), 1.59 (d, *J* = 7.5 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.3, 155.5, 140.2, 137.2, 131.1, 129.4, 129.0, 128.3, 127.8, 127.3, 123.4, 118.6, 113.2, 53.7, 21.5.

MS (EI): *m*/*z* (%) = 263 (90) [M^+], 221 (100), 193 (60).

Cyclopropyl-2-phenyl-1*H*-quinolin-4-one (3ae)
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), cyclopropanamine (85.7 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 2 h gave **3ae**.

Yield: 115.1 mg (88%); white solid; mp 173–175 °C.

IR (KBr): 3485, 3384, 3313, 2925, 2854, 1613, 1594, 1554 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 8.0 Hz, 1 H), 7.95 (d, *J* = 8.5 Hz, 1 H), 7.68 (t, *J* = 8.0 Hz, 1 H), 7.50–7.45 (m, 5 H), 7.37 (t, *J* = 7.0 Hz, 1 H), 6.30 (s, 1 H), 3.33 (t, *J* = 3.5 Hz, 1 H), 0.92 (d, *J* = 6.0 Hz, 2 H), 0.54 (d, *J* = 3.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.3, 155.7, 143.2, 136.9, 131.8, 129.3, 128.6, 128.4, 126.7, 126.4, 123.7, 118.0, 113.3, 32.5, 13.0.

MS (EI): *m*/*z* (%) = 261 (63) [M^+], 260 (100), 232 (32).

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.62; H, 5.84; N, 5.29.

Cyclohexyl-2-phenyl-1*H*-quinolin-4-one (3af)[20]
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), cyclohexanamine (148.8 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 10 h gave **3af**.

Yield: 80.1 mg (53%); white solid; mp 200–202 °C.

IR (KBr): 3443, 2936, 2849, 1627, 1592, 764 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.50 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.95 (d, *J* = 9.0 Hz, 1 H), 7.63–7.60 (m, 1 H), 7.49–7.47 (m, 3 H), 7.39–7.35 (m, 3 H), 6.21 (s, 1 H), 4.14 (tt, *J* = 7.5, 3.5 Hz, 1 H), 2.44–2.37 (m, 2 H), 1.86–1.79 (m, 4 H), 1.61–1.59 (m, 1 H), 1.24–1.13 (m, 1 H), 1.03–0.94 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.4, 155.8, 141.1, 137.4, 131.0, 129.5, 128.9, 128.2, 127.7, 127.2, 123.4, 119.0, 113.4, 63.6, 31.2, 26.6, 25.2.

MS (EI): *m*/*z* (%) = 303 (39) [M^+], 221 (100).

1-(2-Hydroxyethyl)-2-phenyl-1*H*-quinolin-4-one (3ag)
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), 2-aminoethanol (36.7 mg, 0.75 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 2 h gave **3ag**.

Yield: 125.0 mg (94%); white solid; mp 218–220 °C.

IR (KBr): 3204, 2920, 2868, 1618, 1596, 1563, 1054 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.25 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.87 (d, *J* = 8.5 Hz, 1 H), 7.78–7.75 (m, 1 H), 7.55–7.50 (m, 5 H), 7.43 (t, *J* = 7.5 Hz, 1 H), 5.91 (s, 1 H), 4.88 (t, *J* = 5.5 Hz, 1 H), 4.17 (t, *J* = 6.5 Hz, 2 H), 3.54 (q, *J* = 6.5 Hz, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 175.5, 155.1, 140.7, 136.1, 132.2, 129.2, 128.63, 128.57, 126.8, 125.6, 123.4, 117.7, 111.7, 58.3, 49.4.

MS (EI): *m*/*z* (%) = 265 (48) [M^+], 234 (100).

Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.70; H, 5.80; N, 5.38.

Benzyl-2-phenyl-1*H*-quinolin-4-one (3ah)[20]
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), benzylamine (80.4 mg, 0.75 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 2 h gave **3ah**.

Yield: 149.3 mg (96%); white solid; mp 159–161 °C.

IR (KBr): 1629, 1600, 1546, 1484, 1467, 1418 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 8.0 Hz, 1 H), 7.52–7.49 (m, 1 H), 7.44–7.41 (m, 1 H), 7.37–7.32 (m, 6 H), 7.30–7.23 (m, 3 H), 6.98 (d, *J* = 7.5 Hz, 2 H), 6.34 (s, 1 H), 5.27 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.7, 155.1, 141.1, 136.4, 135.6, 132.4, 129.7, 129.0, 128.7, 128.1, 127.6, 127.2, 126.8, 125.5, 123.8, 117.3, 113.1, 52.2.

MS (EI): *m*/*z* (%) = 311 (50) [M^+], 91 (100).

2-Phenyl-1-propenyl-1*H*-quinolin-4-one (3ai)
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), allylamine (85.7 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4.5 h gave **3ai**.

Yield: 95.3 mg (72%); yellow solid; mp 159–161 °C.

IR (KBr): 1629, 1600, 1546, 1484, 1467, 1418 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.47 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.63–7.60 (m, 1 H), 7.52–7.50 (m, 1 H), 7.44–7.35 (m, 6 H), 6.38 (dd, *J* = 7.0, 1.5 Hz, 1 H), 6.35 (s, 1 H), 5.76 (dq, *J* = 7.0, 1.5 Hz, 1 H), 1.28 (dd, *J* = 7.0, 1.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1, 154.0, 141.1, 136.0, 132.3, 130.6, 129.4, 128.7, 128.1, 127.3, 126.6, 126.2, 123.9, 117.3, 112.4, 12.6.

MS (EI): *m*/*z* (%) = 261 (100) [M^+].

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.38; H, 5.79; N, 5.45.

1,2-Diphenyl-1*H*-quinolin-4-one (3aj)[11a]
Following the same procedure used for **3aa** with **1k** (120.4 mg, 0.5 mmol), aniline (140.0 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 11 h gave **3aj**.

Yield: 11.5 mg (8%); yellow solid; mp 270–272 °C.

IR (KBr): 1628, 1594, 1403, 1310, 701 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.52 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.49–7.46 (m, 1 H), 7.40–7.31 (m, 4 H), 7.21–7.14 (m, 7 H), 6.91 (d, *J* = 8.5 Hz, 1 H), 6.44 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1, 154.1, 142.7, 139.2, 135.8, 132.0, 130.1, 129.7, 129.3, 129.0, 128.7, 128.0, 126.3, 126.2, 123.9, 118.2, 112.6.

MS (EI): *m*/*z* (%) = 297 (44) [M^+], 149 (30), 105 (78), 55 (100).

Butyl-2-(4-methoxy-phenyl)-1*H*-quinolin-4-one (3ba)
Following the same procedure used for **3aa** with **1b** (135.0 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 3.5 h gave **3ba**.

Yield: 153.0 mg (99%); yellow solid; mp 129–131 °C.

IR (KBr): 2958, 2932, 2872, 2838, 1624, 1600, 1509, 1485, 1421, 1380, 840 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.50 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.69–7.65 (m, 1 H), 7.53 (d, *J* = 8.5 Hz, 1 H), 7.39 (d, *J* = 8.0 Hz, 1 H), 7.36 (d, *J* = 0.5 Hz, 2 H), 7.32–7.29 (m, 2 H), 6.22 (s, 1 H), 4.04 (t, *J* = 7.5 Hz, 2 H), 3.87 (s, 3 H), 1.63 (quint, *J* = 7.5 Hz, 2 H), 1.19–1.11 (m, 2 H), 0.76 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.5, 160.4, 154.7, 140.8, 132.2, 129.8, 128.5, 127.4, 127.1, 123.6, 116.4, 114.2, 113.2, 55.5, 48.0, 30.9, 19.8, 13.6.

MS (EI): *m*/*z* (%) = 307 (87) [M^+], 264 (100).

Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.22; H, 6.82; N, 4.51.

Butyl-2-(4-ethylphenyl)-1*H*-quinolin-4-one (3ca)
Following the same procedure used for **3aa** with **1c** (138.0 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 6 h gave **3ca**.

Yield: 153.6 mg (98%); yellow solid; mp 90–91 °C.

IR (KBr): 2962, 2931, 2872, 1626, 1599, 1509, 1484, 1466, 1420, 1378, 840 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.49 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.68–7.64 (m, 1 H), 7.52 (d, *J* = 8.5 Hz, 1 H), 7.37 (t, *J* = 7.5 Hz, 1 H), 7.29 (AA′ of AA′BB′, *J* = 8.5 Hz, 2 H), 7.27 (BB′ of AA′BB′, *J* = 9.0 Hz, 2 H), 6.22 (s, 1 H), 4.02 (t, *J* = 8.0 Hz, 2 H), 2.71 (q, *J* = 8.0 Hz, 2 H), 1.62 (quint, *J* = 7.5 Hz, 2 H), 1.28 (t, *J* = 7.5 Hz, 3 H), 1.17–1.10 (m, 2 H), 0.735 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.5, 155.0, 145.8, 140.7, 133.4, 132.2, 128.4, 128.2, 127.4, 127.1, 123.5, 116.4, 112.9, 48.0, 30.8, 28.8, 19.7, 15.4, 13.5.

MS (EI): *m*/*z* (%) = 305 (74) [M^+], 234 (62), 149 (71), 133 (77), 57 (100).

Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.44; H, 7.53; N, 4.53.

Butyl-2-(4-fluorophenyl)-1*H*-quinolin-4-one (3da)
Following the same procedure used for **3aa** with **1d** (129.4 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4 h gave **3da**.

Yield: 146.1 mg (98%); yellow solid; mp 99–101 °C.

IR (KBr): 2960, 2932, 2872, 1626, 1598, 1507, 1485, 1467, 1421, 844, 761 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.48 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.70–7.66 (m, 1 H), 7.52 (d, *J* = 8.5 Hz, 1 H), 7.40–7.36 (m, 3 H), 7.20–7.16 (m, 2 H), 6.20 (s, 1 H), 3.99 (t, *J* = 7.5 Hz, 2 H), 1.63 (quint, *J* = 7.5 Hz, 2 H), 1.19–1.12 (m, 2 H), 0.76 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.3, 163.1 (d, $^1J_{C–F}$ = 248.8 Hz), 153.5, 140.6, 132.3, 132.1 (d, $^4J_{C–F}$ = 3.75 Hz), 130.4 (d, $^3J_{C–F}$ = 8.75 Hz), 127.3, 127.1, 123.7, 116.3, 115.9 (d, $^2J_{C–F}$ = 21.25 Hz), 113.1, 47.9, 30.8, 19.7, 13.4.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –110.9 (s, Ar-F).

MS (EI): *m*/*z* (%) = 295 (50) [M^+], 252 (100), 57 (100), 55 (80).

Anal. Calcd for $C_{19}H_{18}FNO$: C, 77.27; H, 6.14; N, 4.74. Found: C, 77.22; H, 6.11; N, 4.69.

1-Butyl-2-(4-chlorophenyl)-1*H*-quinolin-4-one (3ea)
Following the same procedure used for **3aa** with **1e** (137.6 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4 h gave **3ea**.

Yield: 125.3 mg (80%); yellow solid; mp 112–113 °C.

IR (KBr): 2958, 2930, 2871, 1624, 1601, 1483, 1420, 1090, 840, 760 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.51 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.71–7.68 (m, 1 H), 7.54–7.52 (m, 1 H), 7.49–7.47 (m, 2 H), 7.42–7.33 (m, 3 H), 6.19 (s, 1 H), 3.99 (t, *J* = 7.5 Hz, 2 H), 1.63 (quint, *J* = 7.5 Hz, 2 H), 1.20–1.13 (m, 2 H), 0.78 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.4, 153.4, 140.7, 136.0, 134.6, 132.5, 129.9, 129.2, 127.5, 127.2, 123.8, 116.4, 113.1, 48.1, 30.9, 19.82, 13.6.

MS (EI): *m*/*z* (%) = 313 (21) [M^+ (^{37}Cl)], 311 (64) [M^+ (^{35}Cl)], 233 (100).

Anal. Calcd for $C_{19}H_{18}ClNO$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.20; H, 5.81; N, 4.40.

1-Butyl-2-(3-chlorophenyl)-1*H*-quinolin-4-one (3fa)
Following the same procedure used for **3aa** with **1f** (137.6 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 2 h gave **3fa**.

Yield: 149.8 mg (96%); light-yellow solid; mp 124–126 °C.

IR (KBr): 3051, 2960, 2932, 2869, 1624, 1593, 1570, 1492, 1475, 1427, 779, 762, 742 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 8.0 Hz, 1 H), 7.70–7.66 (m, 1 H), 7.52 (d, *J* = 8.5 Hz, 1 H), 7.48–7.37 (m, 4 H), 7.28 (d, *J* = 7.0 Hz, 1 H), 6.18 (s, 1 H), 3.98 (t, *J* = 7.8 Hz, 2 H), 1.65 (quint, *J* = 7.5 Hz, 2 H), 1.21–1.13 (m, 2 H), 0.76 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.3, 152.9, 140.7, 137.8, 134.9, 132.4, 130.2, 129.8, 128.6, 127.5, 127.2, 126.7, 123.8, 116.3, 113.0, 48.1, 30.9, 19.8, 13.5.

MS (EI): *m*/*z* (%) = 313 (20) [M^+ (^{37}Cl)], 311 (54) [M^+ (^{35}Cl)], 233 (100).

Anal. Calcd for $C_{19}H_{18}ClNO$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.25; H, 5.85; N, 4.50.

2-(3-Chlorophenyl)-1-cyclopropyl-1*H*-quinolin-4-one (3fe)
Following the same procedure used for **3aa** with **1f** (137.6 mg, 0.5 mmol), cyclopropylamine (85.6 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4 h gave **3fe**.

Yield: 133.7 mg (91%); light-yellow solid; mp 173–175 °C.

IR (KBr): 3041, 1627, 1595, 1572, 1475, 753 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 8.0 Hz, 1 H), 7.94 (d, *J* = 8.5 Hz, 1 H), 7.71–7.68 (m, 1 H), 7.52 (s, 1 H), 7.45–7.37 (m, 4 H), 6.26 (s, 1 H), 3.34 (tt, *J* = 7.0, 3.5 Hz, 1 H), 0.98 (d, *J* = 6.5 Hz, 2 H), 0.57 (d, *J* = 3.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.2, 153.9, 143.1, 138.7, 134.6, 132.0, 130.0, 129.5, 128.5, 126.8, 126.6, 126.5, 123.8, 117.9, 113.5, 32.4, 13.1.

MS (EI): *m*/*z* (%) = 297 (18) [M^+ (^{37}Cl)], 295 (65) [M^+ (^{35}Cl)], 294 (100).

Anal. Calcd for $C_{18}H_{14}ClNO$: C, 73.10; H, 4.77; N, 4.74. Found: C, 73.02; H, 4.88; N, 4.59.

1-Butyl-2-(2-chlorophenyl)-1*H*-quinolin-4-one (3ga)
Following the same procedure used for **3aa** with **1g** (137.6 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4 h gave **3ga**.

Yield: 140.6 mg (90%); light-yellow solid; mp 140–143 °C.

IR (KBr): 2960, 2931, 2861, 1623, 1603, 1590, 1490, 1473, 1417, 1183, 754 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.52–8.48 (m, 1 H), 7.69–7.65 (m, 1 H), 7.53–7.48 (m, 2 H), 7.45–7.36 (m, 4 H), 6.17 (s, 1 H), 4.10–4.04 (m, 1 H), 3.74–3.70 (m, 1 H), 1.74–1.71 (m, 1 H), 1.52–1.48 (m, 1 H), 1.18–1.10 (m, 2 H), 0.76–0.70 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.6, 151.3, 140.5, 134.9, 133.0, 132.4, 131.1, 130.7, 130.0, 127.5, 127.3, 127.1, 123.7, 116.3, 112.8, 47.8, 30.5, 19.8, 13.4.

MS (EI): *m*/*z* (%) = 313 (35) [M^+ (^{37}Cl)], 311 (90) [M^+ (^{35}Cl)], 233 (100).

Anal. Calcd for $C_{19}H_{18}ClNO$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.54; H, 5.86; N, 4.63.

1-Butyl-2-pentyl-1*H*-quinolin-4-one (3ha)
Following the same procedure used for **3aa** with **1h** (117.4 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 20 h gave **3ha**.

Yield: 135.7 mg (88%); light-yellow solid; mp 52–54 °C.

IR (KBr): 2957, 2930, 2870, 1628, 1599, 1487, 1467, 1427, 760 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.42 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.63–7.59 (m, 1 H), 7.45 (d, *J* = 8.5 Hz, 1 H), 7.31 (t, *J* = 7.5 Hz, 1 H), 6.23 (s, 1 H), 4.10 (t, *J* = 8.0 Hz, 2 H), 2.65 (t, *J* = 8.0 Hz, 2 H), 1.75–1.65 (m, 4 H), 1.51–1.32 (m, 6 H), 1.00 (t, *J* = 7.5 Hz, 3 H), 0.90 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.7, 154.6, 141.0, 132.0, 127.0, 126.9, 123.2, 115.6, 111.1, 46.1, 34.0, 31.6, 31.0, 28.7, 22.4, 20.1, 14.0, 13.8.

MS (EI): *m*/*z* (%) = 271 (14) [M^+], 200 (42), 79 (100), 57 (42).

Anal. Calcd for $C_{18}H_{25}NO$: C, 79.66; H, 9.28; N, 5.16. Found: C, 79.33; H, 9.16; N, 5.04.

1-Butyl-7-chloro-2-phenyl-1*H*-quinolin-4-one (3ia)
Following the same procedure used for **3aa** with **1i** (137.6 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 4.5 h gave **3ia**.

Yield: 145.4 mg (94%); light-yellow solid; mp 63–65 °C.

IR (KBr): 2967, 2935, 2874, 2858, 1627, 1593, 1502, 1482, 1453, 1436, 770 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.43–8.40 (m, 1 H), 7.49–7.50 (m, 4 H), 7.38–7.32 (m, 3 H), 6.20 (q, *J* = 2.0 Hz, 1 H), 3.95 (t, *J* = 8.0 Hz, 2 H), 1.66–1.62 (m, 2 H), 1.16–1.12 (m, 2 H), 0.77–0.73 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8, 155.0, 141.5, 138.7, 135.8, 129.7, 128.90, 128.88, 128.4, 125.9, 124.3, 116.2, 113.5, 48.1, 30.7, 19.7, 13.5.

MS (EI): *m*/*z* (%) = 313 (1) [M^+ (^{37}Cl)], 311 (2) [M^+ (^{35}Cl)], 230 (93), 147 (100).

Anal. Calcd for $C_{19}H_{18}ClNO$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.49; H, 5.93; N, 4.67.

7-Chloro-1-cyclopropyl-2-phenyl-1*H*-quinolin-4-one (3ie)
Following the same procedure used for **3aa** with **1i** (137.6 mg, 0.5 mmol), cyclopropylamine (85.6 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 2 h gave **3ie**.

Yield: 138.5 mg (94%); light-yellow solid; mp 212–214 °C.

IR (KBr): 3077, 3052, 3013, 1626, 1593, 1453, 1436 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.5 Hz, 1 H), 7.92 (d, *J* = 1.5 Hz, 1 H), 7.51–7.46 (m, 5 H), 7.32 (dd, *J* = 8.5, 1.5 Hz, 1 H), 6.27 (s, 1 H), 3.29 (tt, *J* = 7.0, 3.5 Hz, 1 H), 0.95 (d, *J* = 7.0 Hz, 2 H), 0.56 (d, *J* = 3.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.5, 155.8, 143.9, 138.1, 136.6, 129.4, 128.7, 128.3, 128.1, 125.2, 124.2, 117.7, 113.8, 32.5, 13.0.

MS (EI): *m*/*z* (%) = 297 (34) [M^+ (^{37}Cl)], 295 (99) [M^+ (^{35}Cl)], 294 (100).

Anal. Calcd for $C_{18}H_{14}ClNO$: C, 73.10; H, 4.77; N, 4.74. Found: C, 73.02; H, 4.77; N, 4.62.

7-Chloro-1-cyclopropyl-6-fluoro-1*H*-quinolin-4-one (3je)
Following the same procedure used for **3aa** with **1j** (144.7 mg, 0.5 mmol), cyclopropylamine (85.6 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 1 h gave **3je**.

Yield: 72.2 mg (61%); yellow solid; mp 192–193 °C.

IR (KBr): 1633, 1611, 1589, 1541, 1479, 1289, 1260, 825 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 6.0 Hz, 1 H), 7.94 (d, *J* = 6.0 Hz, 1 H), 7.64 (d, *J* = 7.5 Hz, 1 H), 6.13 (d, *J* = 9.5 Hz, 1 H), 3.36 (tt, *J* = 7.0, 3.5 Hz, 1 H), 1.31–1.27 (m, 2 H), 1.06–1.03 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.6, 154.7 (d, $^1J_{C-F}$ = 247.5 Hz), 142.9, 138.2, 126.6, 126.5 (d, $^3J_{C-F}$ = 5.0 Hz), 118.6, 112.6 (d, $^2J_{C-F}$ = 22.5 Hz), 109.6, 33.9, 8.3.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –120.2 (m, Ar-F).

MS (EI): *m*/*z* (%) = 239 (31) [M^+ (^{37}Cl)], 237 (100) [M^+ (^{35}Cl)].

Anal. Calcd for $C_{12}H_9ClFNO$: C, 60.65; H, 3.82; N, 5.89. Found: C, 60.70; H, 3.90; N, 5.80.

One-Pot Stepwise Synthesis of 1,2-Diphenylquinolin-4(1*H*)-one (3aj)[11a]
*From 1-(2-Chlorophenyl)-3-phenylpropynone (**1a**)*: To an oven-dried, capped tube, **1a** (60.2 mg, 0.25 mmol), aniline (27.9 mg, 0.3 mmol) and DMSO (2.0 mL) were added and the reaction mixture was stirred at 140 °C for 10 h and monitored by TLC. $K_3PO_4·3H_2O$ (99.9 mg, 0.38 mmol) was added and the mixture was stirred for 10.5 h. Upon completion, the reaction mixture was washed with H_2O (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phase was washed with brine (2 × 10 mL) and dried over Na_2SO_4. The solid was filtered off through a thin pad of Celite and the filtrate was evaporated under vacuum to give the crude product that was purified by column chromatography on silica gel (EtOAc–PE, 1:1) to give **3aj**.

Yield: 29.6 mg (41%); yellow solid; mp 270–272 °C.

IR (KBr): 1628, 1594, 1403, 1310, 701 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.52 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.49–7.46 (m, 1 H), 7.40–7.31 (m, 4 H), 7.21–7.14 (m, 7 H), 6.91 (d, *J* = 8.5 Hz, 1 H), 6.44 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1, 154.1, 142.7, 139.2, 135.8, 132.0, 130.1, 129.7, 129.3, 129.0, 128.7, 128.0, 126.3, 126.2, 123.9, 118.2, 112.6.

MS (EI): *m*/*z* (%) = 297 (44) [M^+], 149 (30), 105 (78), 55 (100).

*From 1-(2-Bromophenyl)-3-phenylpropynone (**1k**)*: To an oven-dried, capped tube, **1k** (142.0 mg, 0.5 mmol), aniline (140.0 mg, 1.5 mmol) and DMSO (3.0 mL) were added and the reaction mixture was stirred at 140 °C for 12 h and monitored by TLC. $K_3PO_4·3H_2O$ (99.9 mg, 0.38 mmol) was added and the mixture was stirred for 13.5 h. Upon completion, the reaction mixture was washed with H_2O (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phase was washed with brine (2 × 10 mL) and dried over Na_2SO_4. The solid was filtered off through a thin pad of Celite and the filtrate was evaporated under vacuum to give the crude product that was purified by column chromatography on silica gel (EtOAc–PE, 1:1) to give **3aj**; yield: 115.7 mg (78%).

3-Butylamino-1-(2-chlorophenyl)-3-phenylpropenone (4)[20]
Following the same procedure used for **3aa** with **1a** (120.4 mg, 0.5 mmol), butan-1-amine (109.5 mg, 1.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 3 min gave a mixture of **3aa** (21.2 mg, 16%) and **4** (126.9 mg, 81%) as a light-yellow oil.

IR (film): 3062, 2959, 2931, 2872, 1594, 1569, 1484, 1330, 1258, 1090, 755 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 11.23 (s, 1 H), 7.53–7.50 (m, 1 H), 7.44–7.38 (m, 5 H), 7.37–7.34 (m, 1 H), 7.28–7.23 (m, 2 H), 5.41 (s, 1 H), 3.26–3.24 (m, 2 H), 1.61–1.55 (m, 2 H), 1.41–1.33 (m, 2 H), 0.88 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.1, 166.9, 141.4, 135.3, 130.9, 130.2, 130.0, 129.6, 129.4, 128.6, 127.8, 126.6, 97.3, 44.7, 32.8, 20.0, 13.8.

MS (EI): *m*/*z* (%) = 315 (2) [M^+ (^{37}Cl)], 313 (6) [M^+ (^{35}Cl)], 101 (100).

3aa from Intermediate 4
Following the same procedure used for **3aa** with **4** (156.6 mg, 0.5 mmol) and $K_3PO_4·3H_2O$ (199.7 mg, 0.75 mmol) in DMSO for 2 h, the reaction gave **3aa** as a light-yellow solid (131.8 mg, 94%).

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References

(1) (a) Michael, J. P. *Nat. Prod. Rep.* **1997**, *14*, 605. (b) Fort, D. M.; Litvak, J.; Chen, J. L.; Lu, Q.; Phuan, P.-W.; Cooper, R.; Bierer, D. E. *J. Nat. Prod.* **1998**, *61*, 1528. (c) Oliphant, C. M.; Green, G. M. *Am. Fam. Physician.* **2002**, *65*, 455. (d) Mitscher, L. A. *Chem. Rev.* **2005**, *105*, 559.

(2) For selected examples, see: (a) Li, L.; Wang, H.-K.; Kuo, S.-C.; Wu, T.-S.; Lednicer, D.; Lin, C. M.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **1994**, *37*, 1126. (b) Xia, Y.; Yang, Z.-Y.; Xia, P.; Hackl, T.; Hamel, E.; Mauger, A.; Wu, J.-H.; Lee, K.-H. *J. Med. Chem.* **2001**, *44*, 3932. (c) Hadjeri, M.; Peiller, E.-L.; Beney, C.; Deka, N.; Lawson, M. A.; Dumontet, C.; Boumendjel, A. *J. Med. Chem.* **2004**, *47*, 4964.

(3) For selected examples, see: (a) Llinàs-Brunet, M.; Bailey, M. D.; Ghiro, E.; Gorys, V.; Halmos, T.; Poirier, M.; Rancourt, J.; Goudreau, N. *J. Med. Chem.* **2004**, *47*, 6584. (b) Lucero, B. d. A.; Gomes, C. R. B.; Frugulhetti, I. C. d. P. P.; Faro, L. V.; Alvarenga, L.; de Souza, M. C. B. V.; de Souza, T. M. L.; Ferreira, V. F. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1010. (c) Frutos, R. P.; Haddad, N.; Houpis, I. N.; Johnson, M.; Smith-Keenan, L. L.; Fuchs, V.; Yee, N. K.; Farina, V.; Faucher, A.-M.; Brochu, C.; Haché, B.; Duceppe, J.-S.; Beaulieu, P. *Synthesis* **2006**, 2563.

(4) For selected examples, see: (a) Nakamura, S.; Kozuka, M.; Bastow, K. F.; Tokuda, H.; Nishino, H.; Suzuki, M.; Tatsuzaki, J.; Morris, Natschke. S. L.; Kuo, S.-C.; Lee, K.-H. *Bioorg. Med. Chem. Lett.* **2005**, *13*, 4396. (b) Dubar, F.; Anquetin, G.; Pradines, B.; Dive, D.; Khalife, J.; Biot, C. *J. Med. Chem.* **2009**, *52*, 7954. (c) Dubar, F.; Wintjens, R.; Martins-Duarte, E. S.; Vommaro, R. C.; de Souza, W.; Dive, D.; Pierrot, C.; Pradines, B.; Wohlkonig, A.; Khalife, J.; Biot, C. *Med. Chem. Commun.* **2011**, *2*, 430.

(5) (a) Fouda, A. *Synthesis of New 4-Quinolones of Expected Anticancer Activity: Synthesis, Drug Design and Biological Assay;* Lap Lambert Academic Publishing: Germany, **2010**. For selected reviews, see: (b) Boteva, A.; Krasnykh, O. *Chem. Heterocycl. Compd. (Engl. Transl.)* **2009**, *45*, 757. (c) Mphahlele, M. J. *J. Heterocycl. Chem.* **2010**, *47*, 1.

(6) Ding, D.; Li, X.; Wang, X.; Du, Y.; Shen, J. *Tetrahedron Lett.* **2006**, *47*, 6997.

(7) Huang, J.; Chen, Y.; King, A. O.; Dilmeghani, M.; Larsen, R. D.; Faul, M. M. *Org. Lett.* **2008**, *10*, 2609.

(8) Jones, C. P.; Anderson, K. W.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 7968.

(9) For selected examples, see: (a) Haddad, N.; Tan, J.; Farina, V. *J. Org. Chem.* **2006**, *71*, 5031. (b) Genelot, M.; Dufaud, V.; Djakovitch, L. *Tetrahedron* **2011**, *67*, 976.

(10) (a) Coppola, G. M. *J. Heterocycl. Chem.* **1982**, *19*, 727. (b) Yoshino, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2009**, *131*, 7494.

(11) (a) Zhao, T.; Xu, B. *Org. Lett.* **2010**, *12*, 212. (b) Sun, C.; Xu, B. *J. Org. Chem.* **2008**, *73*, 7361. (c) Wang, C.; Sun, C.; Weng, F.; Gao, M.; Liu, B.; Xu, B. *Tetrahedron Lett.* **2011**, *52*, 2984. (d) Ye, W.; Mo, J.; Zhao, T.; Xu, B. *Chem. Commun.* **2009**, 3246.

(12) Kanzian, T.; Nigst, T. A.; Maier, A.; Pichl, S.; Mayr, H. *Eur. J. Org. Chem.* **2009**, 6379.

(13) Hu, A.; You, T.; Tan, Y.; Wang, Y. *Chin. J. Synth. Chem.* **2006**, *14*, 640.

(14) Reddy, P. G.; Baskaran, S. *Tetrahedron Lett.* **2001**, *42*, 6775.

(15) Audisio, D.; Messaoudi, S.; Peyrat, J.-F. O.; Brion, J.-D.; Alami, M. *J. Org. Chem.* **2011**, *76*, 4995.

(16) Carr, R. M.; Sutherland, D. R. *J. Labelled Compd. Radiopharm.* **1994**, *34*, 961.

(17) For selected examples, see: (a) Almeida, A. I. S.; Silva, A. M. S.; Cavaleiro, J. A. S. *Synlett* **2010**, 462. (b) Cross, R. M.; Monastyrskyi, A.; Mutka, T. S.; Burrows, J. N.; Kyle, D. E.; Manetsch, R. *J. Med. Chem.* **2010**, *53*, 7076.

(18) Venkataraman, S.; Barange, D. K.; Pal, M. *Tetrahedron Lett.* **2006**, *47*, 7317.

(19) (a) Hessian, K. O.; Flynn, B. L. *Org. Lett.* **2005**, *8*, 243. (b) Cross, R. M.; Manetsch, R. *J. Org. Chem.* **2010**, *75*, 8654.

(20) Bernini, R.; Cacchi, S.; Fabrizi, G.; Sferrazza, A. *Synthesis* **2009**, 1209.
(21) For the stereochemistry of intermediate **4**, see: Fuchs, F.; Eller, G.; Holzer, W. *Molecules* **2009**, *14*, 3814.
(22) For the timescale needed for addition of *n*-butylamine to substrate **1a**, see the Supporting Information.
(23) Elbe, H.; Tiemann, R.; Dutzmann, S.; Stenzel, K.; Yuan, L. P.; Cao, Y.; Deng, C. Z. PCT Int. Appl WO9845283, **1997**.
(24) Keivanloo, A.; Bakherad, M.; Bahramian, B.; Rahmani, M.; Taheri, S. A. N. *Synthesis* **2011**, 325.
(25) Karpov, A. S.; Müller, T. J. J. *Org. Lett.* **2003**, *5*, 3451.
(26) Shim, S. C.; Chae, S. A.; Lee, D. Y.; Lim, H. S.; Kalinin, V. N. *J. Korean Chem. Soc.* **1994**, *38*, 774.

