Synthesis N. D. Rode et al. Paper

An Improved Environmentally Friendly Approach to 4-Nitro-, 4-Sulfonyl-, and 4-Aminoquinolines and 4-Quinolones through Conjugate Addition of Nucleophiles to β-(2-Aminophenyl)-α,β-ynones

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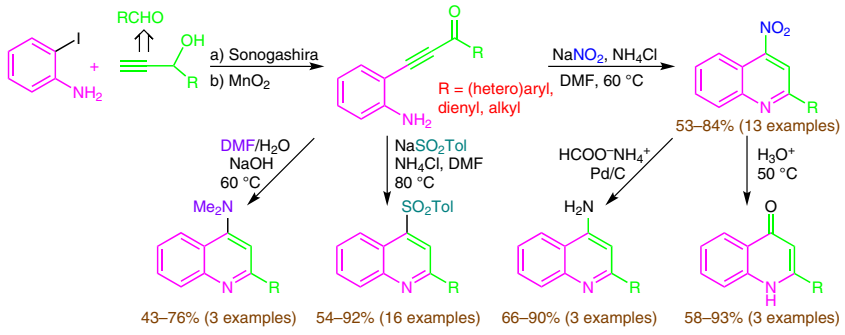

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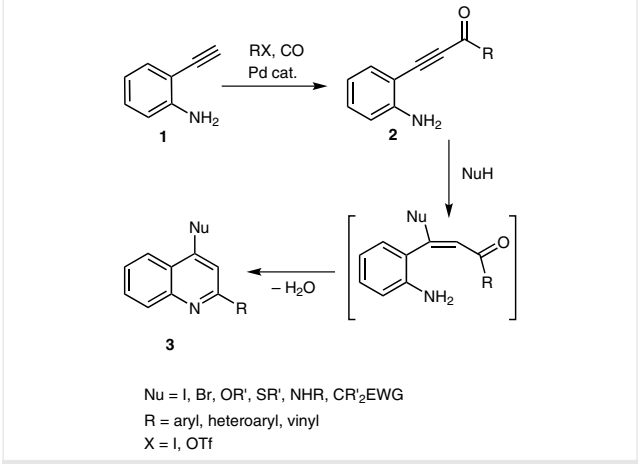
Abstract Sequential addition/annulation reactions of sulfinate and nitrite anions to β-(2-aminophenyl)-α,β-ynones led to valuable 4-sulfonylquinolines and 4-nitroquinolines. The latter proved to be versatile precursors of N-unsubstituted 4-aminoquinolines and 4-quinolones. Reaction of β-(2-aminophenyl)-α,β-ynones with DMF/NaOH resulted in the formation of 4-(dimethylamino)quinolines. The use of an alternative CO-free procedure for the preparation of substrates β-(2-aminophenyl)-α,β-ynones allowed extension of the methodology to the synthesis of 4-substituted 2-alkylquinolines.

Key words nitroquinolines, tosylquinolines, aminoquinolines, quinolones, ynones

Quinoline is one of the most important heterocyclic system, with widespread inclusion in a variety of naturally occurring compounds,[1] and many quinoline derivatives have found application in therapy, for example as antimalarial[2] and anticancer agents.[3] Quinoline-based frameworks also are key intermediates in assembling new materials with interesting electronic properties.[4] We have thoroughly examined the use of β-(2-aminophenyl)-α,β-ynones **2** as building blocks for the synthesis of quinolines by means of a general strategy based on the conversion of the alkyne triple bond into a *cis*-alkene moiety, which subsequently undergoes sequential cyclocondensation.[5] Among the different methodologies we have developed for this transformation,[6,7] conjugate addition of nucleophiles to **2** followed by sequential cycloamination of C=O has emerged as a straightforward and efficient route to 2,4-disubstituted quinolines (Scheme 1).[8] Halo-, alkoxy-, arylthio-, amino-, and EWG-containing alkyl substituents were introduced at the 4-position of the quinoline ring. Nevertheless, some limitations of this procedure should be highlighted. For example, direct conjugate addition of hydroxide ion or ammonia to **2** was quite difficult (*vide infra*). Moreover, the starting ynones **2** were obtained through Pd-catalyzed carbonylative coupling of 2-ethynylaniline with aryl iodides or vinyl triflates. This route requires the reactions to be carried out under CO atmosphere, and restricts the nature of the substituent R to aryl and vinyl groups; consequently, our ynone-based approach to quinolines has not yet been applied to the preparation of 2-alkylquinolines.

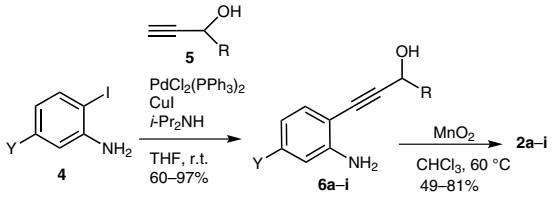


Scheme 1 Previously developed synthesis of quinolines through conjugate addition of nucleophiles to β-(2-aminophenyl)-α,β-ynones **2**

As part of our ongoing interest towards the development of sustainable synthetic procedures for the synthesis of heterocycles,[9] we planned further investigation to over-

come the above limitations and to extend the scope of the sequential conjugate addition to ynones **2** followed by annulation, including different nucleophiles of practical importance. Although the carbonylative coupling reaction allows ready access to **2**, we decided to test also an alternative procedure, involving Sonogashira coupling of 2-iodoaniline **4** (or its substituted analogues) with terminal propargylic alcohols **5** followed by oxidation of the resulting products **6**. Some examples of this approach to **2** (R = Ph, Me, *i*-Pr) through oxidation of **6** with MnO_2[10] or Cr(VI)[11] were previously reported. Thus, ynones **2a–i** (bearing alkyl, as well as aryl, dienyl, and heteroaryl groups) were prepared by oxidation of **6** with MnO_2 (Table 1). Ynones **2j–q** were instead prepared using previously described carbonylative coupling (Figure 1).

Table 1 Synthesis of Ynones **2a–i**



R	Y	4	5	6	Yield (%)	2	Yield (%)
Ph	H	**4a**	**5a**	**6a**	99	**2a**	52
Et	H	**4a**	**5b**	**6b**	96	**2b**	81
n-C_5H_{11}	H	**4a**	**5c**	**6c**	81	**2c**	70
c-Hex	H	**4a**	**5d**	**6d**	83	**2d**	49
$C_4H_9(CH{=}CH)_2$	H	**4a**	**5e**	**6e**	60	**2e**	58
2-furyl	H	**4a**	**5f**	**6f**	97	**2f**	63
2-BrC_6H_4	H	**4a**	**5g**	**6g**	87	**2g**	69
Ph	Cl	**4b**	**5a**	**6h**	95	**2h**	84
Ph	F	**4c**	**5a**	**6i**	95	**2i**	72

Then, we attempted the extension of the scope of our conjugate addition–cyclization methodology to include nitrite and arylsulfinate anions as nucleophiles, with the aim of obtaining interesting 4-nitroquinoline and 4-sulfonylquinoline derivatives **7** and **8**, respectively (Scheme 2).

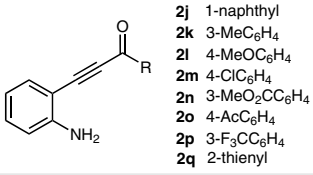
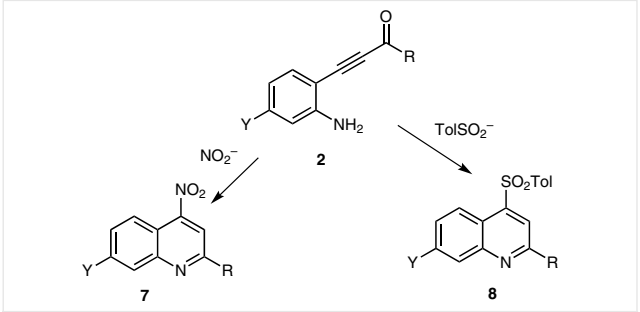


Figure 1 Ynones **2j–q**



Scheme 2 Conjugate addition of nitrite and sulfinate anion to **2**/cyclization

4-Nitroquinolines are useful intermediates. They have found application of as direct precursors of fluorinated imaging agents for detecting neurological disorders[12] and for the synthesis of a trifluoromethylated analogue of ICI D8331.[13]

Interestingly, 4-aminoquinolines[14] and 4-unsubstituted quinolines[15] can also be obtained by selective reduction of 4-nitroquinolines. To the best of our knowledge, preparation of 4-nitroquinolines from acyclic precursors has not been previously reported: the introduction of the 4-nitro group is usually achieved by electrophilic nitration of the quinoline ring, and requires its preliminary activation as the *N*-oxide. One example of displacement of 4-chloroquinoline derivative by nitrite anion has also been described.[16] Both these procedures rely on synthetic elaboration of a preformed quinoline derivative.

4-(Arylsulfonyl)quinoline derivatives showed interesting pharmacological properties as serotonin 5-HT6 receptor antagonists.[17] They also are useful intermediates, since the good leaving ability of $ArSO_2$ group facilitates S_NAr reactions.[18,20a] This characteristic has been employed, for example, in the last step of a large-scale convergent synthesis of the macrocyclic HCV protease inhibitor BI 201302 recently published from a Boehringer-Ingelheim research group.[19] Tosylation of a suitable 4-quinolone, followed by nucleophilic displacement of OTs with sulfinate anion, was used in this case to prepare the target sulfonylquinoline derivative. 4-Sulfonylquinolines were otherwise prepared through reaction of nitroarenes with allyl tolyl sulfones[20] and reaction of indol-3-yl methyl sulfone with nitrobenzene.[21] Oxidation of 7-chloro-4-(*p*-tolylthio)quinoline to the corresponding sulfonyl derivative was also described.[22]

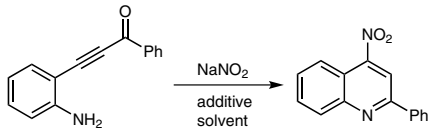
Therefore, new efficient approaches to these significant quinoline derivatives should be beneficial. Herein we report the results of our study.

We started the investigation by exploring the reaction of the nitrite anion with ynones **2**. Conjugate addition of NO_2^- to enones has been described;[23] no examples of similar reactions with ynones have been reported so far. Thus,

reaction between **2a** and $NaNO_2$ was selected as a model system, and the results obtained under different conditions are summarized in Table 2.

When the reaction of **2a** with 2 equiv of sodium nitrite was carried out in DMF at 60 °C in the presence of 2 equivalents of TsOH (this additive was an efficient proton source for the reaction of **2** with NaI),[24] the corresponding quinoline **7a** was obtained only in poor yield (entry 1); worse results were observed by using water as additive and in absence of any additive (entries 2–4). Ammonium chloride in DMF was a more suitable additive, giving **7a** in satisfactory yield (entries 5–8), and the best result was observed at 60 °C (entry 7). Other solvents were less effective than DMF (entries 9–11).

Table 2 Optimization of the Conjugate Addition of $NaNO_2$ to **2a**[a]



2a **7a**

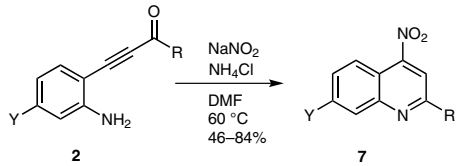
Entry	Solvent	Additive	Temp (°C)	Time (h)	Yield[a,b] (%) of **7a**
1	DMF	TsOH	60	1	24
2	DMF	H_2O	60	10	6
3	DMF	none	100	10	9
4	EtOH	none	80	5	10
5	DMF	NH_4Cl	100	2	43
6	DMF	NH_4Cl	80	2	52
7	**DMF**	**NH_4Cl**	**60**	**2**	**71**
8	DMF	NH_4Cl	r.t.	24	55
9	EtOH	NH_4Cl	60	10	28
10	MeCN	NH_4Cl	60	10	23
11	THF	NH_4Cl	60	24	29

[a] Reaction conditions: **2a** (0.25 mmol), additive (2 equiv), $NaNO_2$ (2 equiv), solvent (1 mL).
[b] Yield of isolated product.

The optimized conditions of entry 7 were used to explore the substrate scope of this sequential conjugate addition of the nitrite anion/cyclization (Table 3).

Ynones **2** bearing aryl moieties containing both electron-donating and electron-withdrawing substituents were converted into the corresponding 2-aryl-4-nitroquinolines in moderate to good yields, and a Cl substituent at the quinoline 7-position was also allowed (entry 5). Heteroaryl groups were also successfully introduced in the target products (entries 3 and 13). In some instances, depending on the nature of the R group, the reaction afforded better results at 40 °C (entries 2 and 3). The scope of the procedure was less general in the case of R = alkyl. For example ynone **2c**, bearing an *n*-pentyl substituent, afforded quinoline **7c** in good yield at 40 °C; however, under the same reaction conditions, a cyclohexyl substituent gave worse results (ynone **2d** was consumed, but we were not able to isolate the expected 2-cyclohexyl-4-nitroquinoline from the complex reaction mixture obtained).

Table 3 Sequential Conjugate Addition of Nitrite to **2**/Cyclization[a]



2 **7**

Entry	**2**	R	Y	**7**	Yield[b] (%)
1	**2a**	Ph	H	**7a**	71
2	**2c**	*n*-C_5H_{11}	H	**7c**	22 (63[c])
3	**2f**	2-furyl	H	**7f**	46 (70[d])
4	**2g**	2-BrC_6H_4	H	**7g**	84
5	**2h**	Ph	Cl	**7h**	72
6	**2j**	1-naphthyl	H	**7j**	68
7	**2k**	3-MeC_6H_4	H	**7k**	62
8	**2l**	4-$MeOC_6H_4$	H	**7l**	69
9	**2m**	4-ClC_6H_4	H	**7m**	65
10	**2n**	3-$MeO_2CC_6H_4$	H	**7n**	53
11	**2o**	4-AcC_6H_4	H	**7o**	78
12	**2p**	3-$F_3CC_6H_4$	H	**7p**	60
13	**2q**	2-thienyl	H	**7q**	68

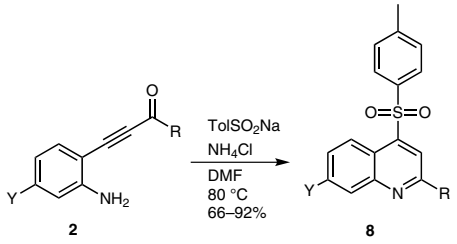
[a] Reaction conditions: molar ratio **2**/$NaNO_2$/NH_4Cl = 1:2:2, 60 °C, 2 h (unless otherwise stated).
[b] Yield of isolated product.
[c] Carried out at 40 °C for 6 h.
[d] Carried out at 40 °C for 3 h.

Next, we extended the procedure to the synthesis of 4-sulfonylquinoline derivatives **8**.

As reported in Table 4, the reaction afforded satisfactory results not only with aryl/heteroaryl substituents, but also with alkyl substituents in the starting ynones (entries 2–4). A dienyl group was also introduced successfully (entry 5).

Although primary amines reacted efficiently with ynones **2** to give N-substituted 4-aminoquinolines,[8b] we failed to obtain 4-aminoquinolines **9** (bearing an unsubstituted NH_2 group) through conjugate addition of NH_3 to **2** using similar conditions. As an example, **9a** was detected in trace amounts when **2a** was reacted with 2 equivalents of 2 M NH_3 in methanol in a screw cap-sealed tube (toluene, 110 °C, 16 h). Selective Pd/C catalyzed reduction of **7** with ammonium formate allowed a convenient preparation of products **9** (Scheme 3).[25]

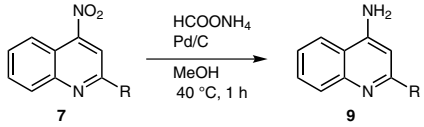
Table 4 Sequential Conjugate Addition of Sulfinate to **2**/Cyclization[a]



2 **8**

Entry	2	R	Y	8	Yield[b] (%)
1	**2a**	Ph	H	**8a**	83
2	**2b**	Et	H	**8b**	54
3	**2c**	*n*-C_5H_{11}	H	**8c**	86
4	**2d**	*c*-Hex	H	**8d**	66[c]
5	**2e**	(*E*,*E*)-octa-1,3-dienyl	H	**8e**	72[c]
6	**2f**	2-furyl	H	**8f**	86
7	**2g**	2-BrC_6H_4	H	**8g**	70
8	**2i**	Ph	F	**8i**	83
9	**2j**	1-naphthyl	H	**8j**	88
10	**2k**	3-MeC_6H_4	H	**8k**	89
11	**2l**	4-MeOC_6H_4	H	**8l**	87
12	**2m**	4-ClC_6H_4	H	**8m**	91
13	**2n**	3-Me$O_2CC_6H_4$	H	**8n**	75
14	**2o**	4-AcC_6H_4	H	**8o**	83
15	**2p**	3-$F_3CC_6H_4$	H	**8p**	92
16	**2q**	2-thienyl	H	**8q**	78

[a] Reaction conditions: molar ratio **2**/$ArSO_2Na$/NH_4Cl = 1:2:2, 80 °C, 2 h (unless otherwise stated).
[b] Yield of isolated product.
[c] Carried out at 50 °C for 1 h.

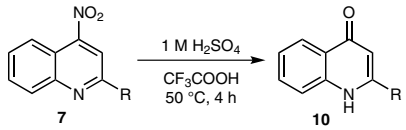


7 **9**

R	9	Yield (%)
Ph	**9a**	89
2-furyl	**9f**	66
4-AcC_6H_4	**9o**	90

Scheme 3 Reduction of **7** to give 4-aminoquinolines **9**

Also conjugate addition of hydroxide ion to **2** to give 4-quinolone derivatives was unsuccessful: we observed a sluggish reaction when **2a** was treated with 2 equivalents of 5% NaOH in MeCN at 60 °C (after 24 h, TLC analysis showed only partial conversion of the starting ynone, with little formation of 2-phenyl-4-quinolone **10a**). Hydrolysis of 4-nitroquinolines[13] allowed a simple alternative route to **10** (Scheme 4).

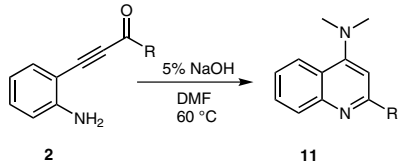


7 **10**

R	10	Yield (%)
Ph	**10a**	93
4-ClC_6H_4	**10m**	58
2-thienyl	**10q**	78

Scheme 4 Hydrolysis of **7** to give 4-quinolones **10**

Surprisingly, an attempt to carry out the addition of NaOH to **2a** using DMF/H_2O (80:20) in place of MeCN resulted in the isolation of 4-(dimethylamino)quinoline **11a** in 71% yield after 1 hour at 60 °C. When the experiment was repeated omitting NaOH, under otherwise identical conditions, only starting material was detected in the reaction mixture, without formation of **11a**. Prolonging the reaction time to 8 hours afforded similar results. These observations support the idea that, under the present reaction conditions, DMF does not act as a nucleophile.[26] Likely, its base-promoted hydrolysis generates dimethylamine, whose reaction with **2a** affords **11a** (the reaction of ynones **2** with secondary amines to give **11** has been reported[8b,27]). The use of DMF in place of dimethylamine to give **11** was briefly explored (Scheme 5).



2 **11**

R	11	Yield (%)
Ph	**11a**	71
n-C_5H_{11}	**11c**	43
4-MeOC_6H_4	**11l**	76

Scheme 5 Reaction of **2** with DMF/NaOH to give 4-(dimethylamino)quinolines **11**

In summary, we have developed a practical route to 4-nitroquinolines **7** and 4-sulfonylquinolines **8** through the reaction of β-(2-aminophenyl)-α,β-ynones **2** with nitrite and sulfinate anions in the presence of cheap ammonium chloride as a proton source. The 4-nitroquinoline derivatives obtained proved to be versatile precursors of interesting 2-aryl-4-quinolones[28] and N-unsubstituted 4-aminoquinolines.[29] DMF/NaOH was demonstrated to be an alternative to the use of dimethylamine for the synthesis of 4-(dimethylamino)quinolines. The preparation of starting ynones using an alternative environmentally friendly CO-free procedure allowed the introduction of alkyl groups (as well as other useful substituents) in the 2-position of the quinoline ring, due to the wide availability of terminal alkynes **5**.

Unless otherwise stated, all starting materials, catalysts, and solvents were commercially available and were used as purchased. Reaction products were purified by flash chromatography on silica gel eluting with *n*-hexane/EtOAc mixtures. 2-iodoanilines **4a–c** and terminal alkynes **5a–c** are commercially available; terminal alkynes **5d**,[30] **5e**,[31] **5f**,[32] and **5g**[33] are known compounds. Propargylic alcohol **6a**[10b] and ynones **2a**,[10b] **2j**,[8a] **2l**,[8a] **2m**,[8a] **2p**,[8a] and **2o**[24] are known compounds. Ynones **2k**, **2n** and **2q** were prepared according to the literature.[6b] Quinolines **7a**,[34] **9a**,[35] **10a**,[28d] **10m**,[28c] **10q**,[28d] **11a**,[26] and **11l**[26] are known compounds and were identified by comparison of their physical and spectral data with those reported in the cited references. Melting points were obtained using a Büchi 500 apparatus and are uncorrected. IR spectra (KBr pellets or neat on NaCl plates) were recorded on a Perkin-Elmer Spectrum Two FT-IR spectrophotometer. ^{1}H NMR spectra were recorded at 400 MHz on a Bruker Avance III spectrometer referenced to TMS (δ = 0) in $CDCl_3$. ^{13}C NMR spectra were obtained using the same instrument at 100.6 MHz and were calibrated with $CDCl_3$ (δ = 77.03). HRMS spectra were recorded using a MALDI-TOF spectrometer: AB SCIEX TOF/TOF 5800 System.

3-(2-Aminophenyl)-1-(*m*-tolyl)prop-2-yn-1-one (2k)

Yellow solid; yield: 0.518 g (58%); mp 119–120 °C.

IR (KBr): 3404, 3312, 2171, 1642, 1623, 1597, 1456, 1154, 738 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–8.04 (m, 2 H), 7.48 (dd, *J* = 1.6, 6.7 Hz, 1 H), 7.38–7.45 (m, 2 H), 7.23–7.28 (m, 1 H), 6.71–6.76 (m, 2 H), 4.52 (s, 2 H, NH_2), 2.45 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 178.02, 150.40, 138.53, 137.07, 134.83, 133.77, 132.59, 129.72, 128.54, 126.99, 117.97, 114.71, 103.94, 93.45, 90.97, 21.35.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{14}NO$: 236.1075; found: 236.1077.

Methyl 3-[3-(2-Aminophenyl)prop-2-ynoyl]benzoate (2n)

Yellow solid; yield: 0.826 g (82%); mp 156–158 °C.

IR (KBr): 3408, 3317, 2175, 1726, 1618, 1434, 1199, 713 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88–8.89 (m, 1 H), 8.37–8.39 (m, 1 H), 8.28–8.30 (m, 1 H), 7.61 (t, *J* = 7.9 Hz, 1 H), 7.51 (dd, *J* = 1.7, 7.9 Hz, 1 H), 7.25–7.30 (m, 1 H), 6.73–6.77 (m, 2 H), 4.57 (br s, 2 H, NH_2), 3.98 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 176.75, 166.12, 150.64, 137.23, 134.59, 134.04, 133.19, 132.96, 130.84, 130.81, 128.93, 118.05, 114.79, 103.48, 93.21, 92.40, 52.49.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}NO_3$: 280.0974; found: 280.0973.

3-(2-Aminophenyl)-1-(thiophen-2-yl)prop-2-yn-1-one (2q)

Brown solid; yield: 1.57 g (92%); mp 131–132 °C.

IR (KBr): 3400, 3321, 2179, 1635, 1589, 1411, 1290, 717 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 1.3, 2.6 Hz, 1 H), 7.76 (dd, *J* = 1.7, 7.9 Hz, 1 H), 7.72 (dd, *J* = 1.3, 3.6 Hz, 1 H), 7.24–7.28 (m, 1 H), 7.19 (dd, *J* = 1.3, 3.6 Hz, 1 H), 6.71–6.75 (m, 2 H), 4.50 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 169.52, 150.36, 144.98, 134.91, 134.58, 133.80, 132.70, 128.41, 118.02, 114.73, 103.85, 92.87, 89.89.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}NOS$: 228.0483; found: 228.0480.

3-(2-Aminophenyl)-1-(2-bromophenyl)prop-2-yn-1-ol (6g); Typical Procedure for the Sonogashira Coupling of 2-Iodoaniline with Alkynes 5a–g

To a solution of 2-iodoaniline (1.000 g, 4.57 mmol) in THF (15 mL) and *i*-Pr_2NH (3.20 mL, 22.83 mmol) were added 1-bromo-2-ethynylbenzene **5g** (1.16 g, 5.48 mmol), $PdCl_2(PPh_3)_2$ (0.048 g, 0.068 mmol, 1.5 mol%), and CuI (0.026 g, 0.136 mmol, 3 mol%). The mixture was stirred at r.t. under N_2 for 2 h. After completion of the reaction, the mixture was extracted with NH_4Cl (0.5 M) and EtOAc (3 ×). The combined organic phases were dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (petroleum ether/EtOAc, 80:20) to give **6g** as a brown oil; yield: 1.205 g (87%).

IR (neat): 3404, 3283, 3009, 2175, 1618, 1589, 1431, 1025, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 1.9, 7.8 Hz, 1 H), 7.58 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.35–7.39 (m, 1 H), 7.29 (dd, *J* = 1.6, 7.9 Hz, 1 H), 7.18–7.22 (m, 1 H), 7.10–7.14 (m, 1 H), 6.65–6.79 (m, 2 H), 6.03 (s, 1 H), 4.20 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 148.09, 139.70, 133.11, 132.31, 130.23, 130.08, 129.93, 128.48, 127.99, 122.54, 117.92, 114.45, 106.95, 93.14, 83.52, 64.81.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}BrNO$: 302.0181; found: 302.0180.

1-(2-Aminophenyl)pent-1-yn-3-ol (6b)

Brown oil; yield: 0.780 g (96%).

IR (neat): 3474, 3371, 2972, 2930, 2220, 1618, 1494, 1456, 1315, 1012, 746 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.26 (m, 1 H), 7.08–7.13 (m, 1 H), 6.65–6.69 (m, 2 H), 4.58 (t, *J* = 6.3 Hz, 1 H), 4.20 (br s, 2 H, NH_2), 1.78–1.86 (m, 2 H), 1.06 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 147.81, 132.24, 129.73, 117.95, 114.42, 107.45, 95.55, 81.45, 64.24, 31.07, 9.60.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{14}NO$: 176.1075; found: 176.1072.

1-(2-Aminophenyl)oct-1-yn-3-ol (6c)

Brown oil; yield: 0.810 g (81%).

IR (neat): 3474, 3366, 2930, 2856, 2220, 1618, 1494, 1456, 1315, 1016, 746 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (dd, *J* = 1.7, 8.1 Hz, 1 H), 7.08–7.12 (m, 1 H), 6.65–6.69 (m, 2 H), 4.62 (t, *J* = 6.6 Hz, 2 H), 4.20 (br s, 1 H, NH_2), 1.74–1.84 (m, 2 H), 1.47–1.54 (m, 2 H), 1.28–1.35 (m, 4 H), 0.90 (t, *J* = 6.7 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 147.79, 132.21, 129.70, 117.94, 114.42, 107.48, 95.86, 81.33, 63.02, 37.98, 31.45, 25.00, 22.56, 14.00.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}NO$: 218.1545; found: 218.1545.

3-(2-Aminophenyl)-1-cyclohexylprop-2-yn-1-ol (6d)

Brown solid; yield: 0.553 g (83%); mp 104–106 °C.

IR (KBr): 3382, 3295, 2845, 2177, 1624, 1495, 1295, 1025, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.28 (m, 1 H), 7.09–7.14 (m, 1 H), 6.66–6.70 (m, 2 H), 4.43 (d, *J* = 6.1 Hz, 1 H), 4.19 (br s, 2 H, NH_2), 1.91–1.95 (m, 1 H), 1.78–1.81 (m, 2 H), 1.62–1.72 (m, 2 H), 1.11–1.30 (m, 6 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): 147.83, 132.30, 129.72, 117.93, 114.37, 107.49, 94.70, 82.29, 67.83, 44.30, 28.76, 28.29, 26.40, 25.92, 25.89.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}NO$: 230.1545; found: 230.1542.

(4*E*,6*E*)-1-(2-Aminophenyl)undeca-4,6-dien-1-yn-3-ol (6e)

Brown oil; yield: 0.418 g (60%).

IR (neat): 3368, 3024, 2926, 2218, 1613, 1455, 1316, 1158, 748 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (dd, *J* = 8.2, 1.9 Hz, 1 H), 7.09–7.13 (m, 1 H), 7.65–7.69 (m, 2 H), 7.42 (dd, *J* = 15.50, 10.2 Hz, 1 H), 6.03–6.09 (m, 1 H), 5.73–5.81 (m, 2 H), 5.16 (d, *J* = 6.1 Hz, 1 H), 4.17 (br s, 2 H, NH_2), 2.10 (q, *J* = 6.9 Hz, 2 H), 1.28–1.39 (m, 4 H), 0.89 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): 147.93, 137.46, 132.67, 132.28, 129.88, 128.86, 128.77, 117.91, 114.43, 107.19, 93.69, 82.71, 63.33, 32.36, 31.24, 22.21, 13.92.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}NO$: 256.1701; found: 256.1700.

3-(2-Aminophenyl)-1-(furan-2-yl)prop-2-yn-1-ol (6f)

Brown solid; yield: 1.90 g (97%); mp 123–124 °C.

IR (KBr): 3408, 2922, 2191, 2171, 1647, 1618, 1386, 1265, 1069 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (dd, *J* = 1.0, 1.9 Hz, 1 H), 7.29 (dd, *J* = 1.5, 8.2 Hz, 1 H), 7.11–7.15 (m, 1 H), 6.66–6.70 (m, 2 H), 6.50 (d, *J* = 3.3 Hz, 1 H), 6.37 (dd, *J* = 1.8, 3.3 Hz, 1 H), 5.72 (s, 1 H), 4.25 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 153.00, 148.21, 143.05, 132.34, 130.20, 117.93, 114.48, 110.52, 107.87, 106.73, 91.68, 82.69, 58.75.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}NO_2$: 214.0868; found: 214.0870.

3-(2-Amino-4-chlorophenyl)-1-phenylprop-2-yn-1-ol (6h)

Brown solid; yield: 1.10 g (95%); mp 82–83 °C.

IR (KBr): 3386, 3307, 3066, 2829, 2210, 1603, 1487, 1420, 1266, 1046, 809 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.1 Hz, 2 H), 7.30–7.39 (m, 3 H), 7.16 (d, *J* = 8.8 Hz, 1 H), 6.61–6.63 (m, 2 H), 5.67 (s, 1 H), 4.27 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 148.96, 140.63, 135.56, 133.20, 128.72, 128.47, 126.61, 118.07, 114.18, 105.60, 95.09, 82.36, 65.04.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}ClNO$: 258.0686; found: 258.0686.

3-(2-Amino-4-fluorophenyl)-1-phenylprop-2-yn-1-ol (6i)

Brown oil; yield: 0.290 g (95%).

IR (neat): 3370, 3066, 2879, 2218, 1624, 1503, 1445, 1283, 1171, 1013, 846, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.57 (m, 2 H), 7.30–7.39 (m, 3 H), 7.21 (dd, *J* = 1.9, 8.1 Hz, 1 H), 6.31–6.38 (m, 2 H), 5.67 (s, 1 H), 4.31 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 163.84 (d, J_{C-F} = 247 Hz), 149.83 (d, J_{C-F} = 12 Hz), 140.71, 133.86 (d, J_{C-F} = 10.7 Hz), 128.70, 128.43, 126.61, 105.19 (d, J_{C-F} = 22.7 Hz), 103.18, 101.19 (d, J_{C-F} = 25.7 Hz), 94.00, 82.49, 65.05.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}FNO$: 242.0981; found: 242.0981.

β-(2-Aminophenyl)-α,β-ynones 2a–i; General Procedure

This transformation was carried out according to ref. 10a. Propargylic alcohol **6** (4–10 mmol) was dissolved in $CHCl_3$ (10–25 mL) and activated MnO_2 (5 equiv) was added. The heterogeneous mixture was refluxed for 3–5 h; the reaction progress was monitored by TLC. When the conversion of starting material was complete, the crude mixture was filtered through a short pad of Celite using EtOAc as eluent. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc mixtures).

1-(2-Aminophenyl)pent-1-yn-3-one (2b)

Brown oil; yield: 0.630 g (81%).

IR (neat): 3470, 3366, 2980, 2935, 2175, 1660, 1622, 1490, 1460, 1315, 1116, 1045, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.36 (m, 1 H), 7.19–7.23 (m, 1 H), 6.65–6.71 (m, 2 H), 4.47 (br s, 2 H, NH_2), 2.69 (q, *J* = 7.3 Hz, 2 H), 1.21 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 188.28, 150.21, 133.74, 132.47, 117.73, 144.56, 103.43, 93.91, 88.81, 38.60, 8.24.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{12}NO$: 174.0919; found: 174.0920.

1-(2-Aminophenyl)oct-1-yn-3-one (2c)

Brown solid; yield: 0.556 g (70%); mp 52–53 °C.

IR (KBr): 3453, 3341, 2933, 2867, 2177, 1645, 1458, 1325, 1258, 1075, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.2 Hz, 1 H), 7.20–7.24 (m, 1 H), 6.67–6.71 (m, 2 H), 4.45 (br s, 2 H, NH_2), 2.66 (t, *J* = 7.9 Hz, 2 H), 1.71–1.78 (m, 2 H), 1.33–1.36 (m, 4 H), 0.91 (t, *J* = 7.9 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 187.98, 150.20, 133.82, 132.51, 117.85, 114.58, 103.60, 94.23, 88.61, 45.39, 31.15, 24.05, 22.38, 13.87.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}NO$: 216.1388; found: 216.1389.

3-(2-Aminophenyl)-1-cyclohexylprop-2-yn-1-one (2d)

Yellow solid; yield: 0.217 g (49%);[36] mp 92–93 °C.

IR (KBr): 3451, 3348, 2922, 2847, 2181, 1639, 1490, 1258, 1002 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.38 (m, 1 H), 7.20–7.24 (m, 1 H), 6.67–6.71 (m, 2 H), 4.44 (br s, 2 H, NH_2), 2.47–5.54 (m, 1 H), 2.04–2.08 (m, 2 H), 1.79–1.84 (m, 2 H), 1.66–1.71 (m, 1 H), 1.46–1.55 (m, 2 H), 1.21–1.39 (m, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 191.24, 150.15, 133.83, 132.43, 117.85, 114.58, 103.81, 93.56, 89.39, 52.17, 28.52, 25.80, 25.42.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO$: 228.1388; found: 228.1386.

(4*E*,6*E*)-1-(2-Aminophenyl)undeca-4,6-dien-1-yn-3-one (2e)

Brown solid; yield: 0.210 g (58%); mp 66–67 °C.

IR (KBr): 3329, 2959, 2922, 2166, 1635, 1618, 1577, 1319, 1178, 991, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.52 (m, 1 H), 7.38–7.40 (m, 1 H), 7.19–7.24 (m, 1 H), 6.68–6.72 (m, 2 H), 6.28–6.35 (m, 2 H), 6.23 (d, *J* = 15.3 Hz, 1 H), 4.47 (br s, 2 H, NH_2), 2.20–2.25 (m, 2 H), 1.31–1.49 (m, 4 H), 0.92 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 178.21, 150.10, 148.43, 147.72, 133.48, 132.22, 130.00, 128.67, 117.83, 114.64, 104.06, 92.95, 88.92, 32.96, 30.71, 22.23, 13.83.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{20}NO$: 254.1545; found: 254.1545.

3-(2-Aminophenyl)-1-(furan-2-yl)prop-2-yn-1-one (2f)

Yellow solid; yield: 0.828 g (63%); mp 109–111 °C.

IR (KBr): 3395, 3317, 2183, 1618, 1456, 1394, 1004, 742 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.68 (m, 1 H), 7.39–7.43 (m, 2 H), 7.22–7.27 (m, 1 H), 6.69–6.75 (m, 2 H), 6.59–6.61 (m, 1 H), 4.61 (s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.76, 153.30, 150.64, 147.70, 133.66, 132.77, 119.87, 117.86, 114.85, 112.73, 103.37, 92.67, 90.75.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}NO_2$: 212.0712; found: 212.0715.

3-(2-Aminophenyl)-1-(2-bromophenyl)prop-2-yn-1-one (2g)

Yellow solid; yield: 0.818 g (69%); mp 108–109 °C.

IR (KBr): 3401, 3221, 2167, 1637, 1610, 1315, 1007, 730 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (dd, *J* = 1.8, 7.9 Hz, 1 H), 7.70 (dd, *J* = 1.4, 7.9 Hz, 1 H), 7.36–7.47 (m, 3 H), 7.23–7.27 (m, 1 H), 6.69–6.73 (m, 2 H), 4.51 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 177.49, 150.65, 138.16, 134.79, 134.00, 133.15, 132.98, 132.29, 127.47, 120.96, 118.00, 114.68, 103.59, 94.68, 92.82.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}BrNO$: 300.0024; found: 300.0024.

3-(2-Amino-4-chlorophenyl)-1-phenylprop-2-yn-1-one (2h)

Yellow solid; yield: 0.753 g (84%); mp 137–138 °C.

IR (KBr): 3391, 3317, 3200, 2183, 1647, 1598, 1257, 1008, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17–8.20 (m, 2 H), 7.61–7.65 (m, 1 H), 7.49–7.54 (m, 2 H), 7.39 (d, *J* = 8.3 Hz, 1 H), 6.74 (d, *J* = 1.9 Hz, 1 H), 6.69–6.71 (m, 1 H), 4.63 (br s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 177.66, 151.16, 138.64, 136.84, 134.74, 134.11, 129.45, 128.70, 118.37, 114.46, 102.35, 93.85, 90.03.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}ClNO$: 256.0529; found: 256.0530.

3-(2-Amino-4-fluorophenyl)-1-phenylprop-2-yn-1-one (2i)

Yellow solid; yield: 205 mg (72%); mp 158–160 °C.

IR (KBr): 3400, 3321, 2183, 1639, 1568, 1452, 1282, 1012, 725 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.3 Hz, 2 H), 7.63 (t, *J* = 7.4 Hz, 1 H), 7.45–7.54 (m, 3 H), 6.42–6.48 (m, 2 H), 4.67 (br s, 2 H, NH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 177.73, 165.68 (d, $^1J_{C-F}$ = 252 Hz), 152.39 (d, $^3J_{C-F}$ = 13 Hz), 136.95, 135.90 (d, $^3J_{C-F}$ = 11 Hz), 134.05, 129.44, 128.69, 105.96 (d, $^2J_{C-F}$ = 23.8 Hz), 101.32 (d, $^2J_{C-F}$ = 24.7 Hz), 100.12 (d, $^4J_{C-F}$ = 2.3 Hz), 93.41, 90.44.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}FNO$: 240.0825; found: 240.0824.

4-Nitro-2-phenylquinoline (7a); Typical Procedure for 2-Substituted 4-Nitroquinolines 7a–q

To a mixture of 3-(2-aminophenyl)-1-phenylprop-2-yn-1-one (**2a**, 0.200 g, 0.90 mmol), $NaNO_2$ (0.125 g, 1.80 mmol), and NH_4Cl (0.097 g, 1.80 mmol) was added DMF (3 mL). The mixture was stirred at 60 °C for 2 h, then extracted with water and EtOAc (3 ×). The combined organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/EtOAc 90:10) to give **7a**; yield: 160 mg (71%)

4-Nitro-2-pentylquinoline (7c)

Brown liquid; yield: 36 mg (63%).

IR (neat): 3408, 2955, 2930, 2860, 1622, 1535, 1353, 767 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35–8.38 (m, 1 H), 8.16–8.18 (m, 1 H), 7.80–7.84 (m, 2 H), 7.67–7.71 (m, 1 H), 3.05–3.09 (m, 2 H), 1.83–1.90 (m, 2 H), 1.38–1.43 (m, 4 H), 0.92 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 163.28, 152.76, 150.01, 130.80, 129.62, 128.76, 122.58, 117.22, 115.32, 39.11, 31.57, 29.24, 22.50, 13.97.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{14}H_{16}KN_2O_2$: 283.0849; found: 283.0850.

2-(Furan-2-yl)-4-nitroquinoline (7f)

Yellow solid; yield: 56 mg (70%); mp 103–105 °C.

IR (KBr): 3425, 3138, 1611, 1588, 1525, 1348, 1088, 1020, 761 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34–8.36 (m, 1 H), 8.33 (s, 1 H), 8.20–8.23 (m, 1 H), 7.83 (ddd, *J* = 8.5, 7.10, 1.4 Hz, 1 H), 7.67–7.71 (m, 2 H), 7.34 (dd, *J* = 3.5, 0.8 Hz, 1 H), 6.64 (dd, *J* = 3.6, 1.8 Hz, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 152.26, 150.27, 148.91, 145.10, 145.09, 131.28, 129.98, 129.10, 122.74, 117.47, 112.78, 111.87, 111.72.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{13}H_8KN_2O_3$: 279.0172; found: 279.0170.

2-(2-Bromophenyl)-4-nitroquinoline (7g)

Pale yellow solid; yield: 48 mg (84%); mp 146–147 °C.

IR (KBr): 3420, 3066, 1603, 1528, 1366, 1341, 1237, 1025, 749 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 7.3 Hz, 1 H). 8.30–8.33 (m, 2 H), 7.87–7.92 (m, 1 H), 7.78–7.82 (m, 1 H), 7.69–7.76 (m, 2 H), 7.48–7.52 (m, 1 H), 7.37 (ddd, *J* = 7.9, 1.9 Hz, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 117.1, 117.7, 121.76, 122.76, 128.01, 129.94, 130.42, 130.98, 131.14, 131.65, 133.61, 139.68, 150.08, 152.08, 158.5.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{15}H_9BrKN_2O_2$: 366.9484; found: 366.9484.

7-Chloro-4-nitro-2-phenylquinoline (7h)

Yellow solid; yield: 40 mg (72%); mp 220–222 °C.

IR (KBr): 3429, 3051, 1617, 1488, 1530, 1354, 1081, 911, 820 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33–8.36 (m, 2 H), 8.22–8.23 (m, 1 H), 8.14–8.16 (m, 2 H), 7.61–7.64 (m, 1 H), 7.51–7.56 (m, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 158.27, 153.03, 150.62, 137.36, 137.02, 130.88, 130.17, 129.21, 129.18, 127.43, 124.14, 115.99, 113.16,

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{15}H_9ClKN_2O_2$: 322.9990; found: 322.9991.

2-(Naphthalen-1-yl)-4-nitroquinoline (7j)

Pale yellow solid; yield: 37 mg (68%); mp 131–132 °C.

IR (KBr): 3412, 3088, 3042, 1604, 1521, 1336, 1236, 1143, 900, 766 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.49–8.51 (m, 1 H), 8.34–8.37 (m, 1 H), 8.27 (s, 1 H), 8.14–8.17 (m, 1 H), 7.90–8.03 (m, 3 H), 7.76–7.83 (m, 2 H), 7.63 (t, *J* = 8.1 Hz, 1 H), 7.51–7.58 (m, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 117.24, 117.49, 122.73, 124.97, 125.40, 126.41, 127.30, 128.36, 128.72, 129.71, 131.28, 130.46, 130.85, 131.26, 134.11, 136.63, 150.30, 152.85, 159.45.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{19}H_{12}KN_2O_2$: 339.0536; found: 339.0535.

4-Nitro-2-(*m*-tolyl)quinoline (7k)

Pale yellow solid; yield: 35 mg (62%); mp 92–93 °C.

IR (KBr): 3425, 3088, 2922, 1602, 1527, 1370, 1309, 1153, 891, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.37–8.41 (m, 2 H), 8.28 (d, *J* = 8.3 Hz, 1 H), 8.02 (s, 1 H), 7.96 (d, *J* = 8.3 Hz, 1 H), 7.84 (t, *J* = 8.3 Hz, 1 H), 7.71 (t, *J* = 8.3 Hz, 1 H), 7.44 (t, *J* = 8.0 Hz, 1 H), 7.33 (d, *J* = 8.0 Hz, 1 H), 2.49 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 157.38, 153.27, 150.34, 138.94, 137.56, 131.30, 131.04, 130.69, 130.38, 129.25, 129.05, 128.06, 124.61, 124.28, 122.65, 117.55, 113.18, 21.56.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{16}H_{12}KN_2O_2$: 303.0536; found: 303.0536.

2-(4-Methoxyphenyl)-4-nitroquinoline (7l)

Yellow solid; yield: 38 mg (69%); mp 104–105 °C.

IR (KBr): 3429, 3096, 2968, 2835, 2366, 1606, 1522, 1357, 1249, 1176, 1034, 766 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.37–8.39 (m, 1 H), 8.36 (s, 1 H), 8.23–8.25 (m, 1 H), 8.18 (d, *J* = 8.2 Hz, 2 H), 7.83 (ddd, *J* = 8.4, 7.00, 1.4 Hz, 1 H), 7.68 (ddd, *J* = 8.4, 6.95, 1.4 Hz, 1 H), 7.08 (d, *J* = 8.2 Hz, 2 H), 3.90 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 161.78, 156.78, 153.34, 150.40, 131.01, 130.21, 128.94, 128.87, 122.66, 117.29, 114.58, 112.62, 55.50.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{16}H_{12}KN_2O_3$: 319.0485; found: 319.0485.

2-(4-Chlorophenyl)-4-nitroquinoline (7m)

Yellow solid; yield: 36 mg (65%); mp 182–183 °C.

IR (KBr): 3416, 2925, 1591, 1520, 1486, 1368, 1091, 1011, 765 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.38–8.43 (m, 2 H), 8.26–8.29 (m, 1 H), 8.16 (d, *J* = 8.7 Hz, 2 H), 7.85–7.89 (m, 1 H), 7.74 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1 H), 7.53 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 1.55.89, 150.38, 136.93, 136.03, 131.29, 130.42, 129.59, 129.42, 129.41, 128.72, 128.71, 122.73, 117.66, 112.68,

HRMS MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_9ClN_2NaO_2$: 307.0250; found: 307.0248.

Methyl 3-(4-Nitroquinolin-2-yl)benzoate (7n)

Yellow solid; yield: 29 mg (53%); mp 140–142 °C.

IR (KBr): 3426, 3083, 2958, 1726, 1526, 1437, 1283, 1236, 1108 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.84–8.85 (m, 1 H), 8.42–8.47 (m, 3 H), 8.31–8.33 (m, 1 H), 8.19–8.21 (m, 1 H), 7.89 (ddd, *J* = 8.5, 7.10, 1.4 Hz, 1 H), 7.74–7.78 (m, 1 H), 7.66 (t, *J* = 8.3 Hz, 1 H), 4.00 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.64, 156.04, 150.38, 137.94, 131.76, 131.46, 131.33, 131.20, 130.51, 129.73, 129.38, 128.49, 122.73, 117.76, 112.93, 52.45.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{17}H_{12}KN_2O_4$: 347.0434; found: 347.0434.

1-[4-(4-Nitroquinolin-2-yl)phenyl]ethan-1-one (7o)

White solid; yield: 43 mg (78%); mp 184–185 °C.

IR (KBr): 3425, 3084, 1680, 1574, 1532, 1423, 1356, 1265, 767 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.43–8.46 (m, 2 H), 8.31–8.33 (m, 3 H), 8.13–8.15 (d, *J* = 8.5 Hz, 2 H), 7.90 (ddd, *J* = 8.5, 7.10, 1.4 Hz, 1 H), 7.78 (ddd, *J* = 8.5, 7.10, 1.4 Hz, 1 H), 2.69 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 197.56, 155.82, 153.47, 150.44, 141.57, 138.32, 131.40, 130.62, 129.97, 129.09, 127.66, 122.76, 177.67, 113.10, 29.73, 26.84.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{17}H_{12}KN_2O_3$: 331.0485; found: 331.0487.

4-Nitro-2-[3-(trifluoromethyl)phenyl]quinoline (7p)

Yellow solid; yield: 33 mg (60%); mp 126–128 °C.

IR (KBr): 3420, 3080, 2852, 1605, 1520, 1405, 1324, 1234, 1117, 931, 771 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.52 (m, 1 H), 8.30–8.44 (m, 4 H), 7.89 (ddd, *J* = 8.4, 7.00, 1.4 Hz, 1 H), 7.74–7.79 (m, 2 H), 7.67–7.71 (m, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 155.40, 153.55, 150.38, 138.33, 131.77 (q, $^2J_{C\text{-}F}$ = 33.00 Hz), 131.44, 130.55, 130.52 (q, $^4J_{C\text{-}F}$ = 1.4 Hz), 129.93, 129.68, 127.03 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.37 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.00 (q, $^1J_{C\text{-}F}$ = 273 Hz), 122.74, 117.83, 112.70,

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{16}H_9F_3KN_2O_2$: 357.0253; found: 357.0253.

4-Nitro-2-(thiophen-2-yl)quinoline (7q)

Yellow solid; yield: 38 mg (68%); mp 114–116 °C.

IR (KBr): 3416, 2925, 1606, 1522, 1425, 1356, 1239, 1067, 771 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.31–8.33 (m, 1 H), 8.24 (s, 1 H), 8.14–8.17 (m, 1 H), 7.74–7.81 (m, 2 H), 7.65 (ddd, *J* = 8.5, 6.9, 1.3 Hz, 1 H), 7.52 (dd, *J* = 1.3, 4.9 Hz, 1 H), 7.16 (dd, *J* = 3.8, 4.9 Hz, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 153.03, 152.22, 150.12, 143.38, 131.20, 130.15, 129.86, 128.96, 128.43, 127.21, 122.68, 117.46, 111.99.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{13}H_8KN_2O_2S$: 294.9944; found: 294.9940.

2-Phenyl-4-tosylquinoline (8a); Typical Procedure for 2-Substituted 4-Tosylquinolines 8a–q

To a mixture of 3-(2-aminophenyl)-1-phenylprop-2-yn-1-one (**2a**, 0.200 g, 0.90 mmol), sodium *p*-toluenesulfinate (0.323 g, 1.80 mmol), and NH_4Cl (0.097 g, 1.80 mmol) was added DMF (3 mL). The mixture was stirred at 80 °C for 2 h, then extracted with water and EtOAc (3 ×). The combined organic phases were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/EtOAc 90:10) to give **8a** as a brown solid; yield: 269 mg (83%); mp 171–173 °C.

IR (KBr): 3441, 3059, 1579, 1490, 1446, 1315, 1145, 1087, 815, 749 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1 H), 8.60–8.62 (m, 1 H), 8.22–8.26 (m, 3 H), 7.91 (d, *J* = 8.3 Hz, 2 H), 7.75 ddd, *J* = 8.4, 7.9, 1.4 Hz, 1 H), 7.52–7.62 (m, 4 H), 7.30 (d, *J* = 8.2 Hz, 2 H), 2.38 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 156.78, 149.63, 145.86, 145.01, 138.15, 137.50, 130.82, 130.49, 130.27, 130.08, 129.11, 128.27, 127.95, 127.60, 124.10, 121.08, 119.27, 21.62.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{22}H_{17}KNO_2S$: 398.0617; found: 398.0620.

2-Ethyl-4-tosylquinoline (8b)

Brown solid; yield: 48 mg (54%); mp 126–127 °C.

IR (KBr): 3432, 2971, 2925, 1594, 1494, 1321, 1146, 1084, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.54–8.57 (m, 1 H), 8.09–8.11 (m, 2 H), 7.88 (d, *J* = 8.3 Hz, 2 H), 7.71 (ddd, *J* = 8.5, 7.10, 1.3 Hz, 1 H), 7.56 (ddd, *J* = 8.5, 7.10, 1.3 Hz, 1 H), 7.30 (d, *J* = 8.3 Hz, 2 H), 3.11 (q, *J* = 7.6 Hz, 2 H), 2.38 (s, 3 H), 1.44 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 163.59, 149.26, 145.25, 144.93, 137.52, 130.18, 130.03, 129.96, 127.88, 127.69, 124.06, 121.22, 120.70, 32.34, 21.60, 13.56.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{18}H_{17}KNO_2S$: 350.0617; found: 350.0619.

2-Pentyl-4-tosylquinoline (8c)

Yellow solid; yield: 28 mg (86%); mp 103–104 °C.

IR (KBr): 3441, 3072, 2976, 1638, 1510, 1597, 1383, 1310, 848, 761 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 8.5 Hz, 1 H), 8.08–8.11 (m, 2 H), 7.87 (d, *J* = 8.3 Hz, 2 H), 7.71 (t, *J* = 8.5 Hz, 1 H), 7.55 (t, *J* = 8.5 Hz, 1 H), 7.29 (d, *J* = 8.3 Hz, 2 H), 3.06 (t, *J* = 7.7 Hz, 2 H), 2.37 (s, 3 H), 1.82–1.90 (m, 2 H), 1.36–1.43 (m, 4 H), 0.92 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 162.81, 149.29, 142.10, 144.90, 137.57, 130.15, 130.02, 129.97, 127.87, 127.85, 124.05, 121.62, 120.67, 39.26, 31.62, 29.33, 22.50, 21.58, 13.99.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{21}H_{23}KNO_2S$: 392.1087; found: 392.1087.

2-Cyclohexyl-4-tosylquinoline (8d)

Pale yellow solid; yield: 53 mg (66%); mp 188–190 °C.

IR (KBr): 3425, 3067, 2923, 2848, 2175, 1596, 1494, 1446, 1317, 1143, 1087, 810, 767 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.53–8.55 (m, 1 H), 8.14 (s, 1 H), 8.09–8.11 (m, 1 H), 7.87 (d, *J* = 8.1 Hz, 2 H), 7.70 (ddd, *J* = 8.4, 7.20, 1.4 Hz, 1 H), 7.54 (ddd, *J* = 8.4, 7.20, 1.4 Hz, 1 H), 7.28 (d, *J* = 8.1 Hz, 2 H), 2.97–3.04 (m, 1 H), 2.37 (s, 3 H), 2.04–2.07 (m, 2 H), 1.90–1.95 (m, 2 H), 1.64–1.84 (m, 4 H), 1.43–1.53 (m, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.47, 149.18, 145.16, 144.84, 137.64, 130.12, 130.05, 130.02, 127.84, 127.61, 124.01, 120.86, 120.31, 47.45, 32.56, 26.38, 25.92, 21.59.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{22}H_{23}KNO_2S$: 404.1087; found: 404.1090.

2-[(1*E*,3*E*)-Octa-1,3-dienyl]-4-tosylquinoline (8e)

Brown solid; yield: 82 mg (72%); mp 76–78 °C.

IR (KBr): 3383, 3018, 2964, 2403, 1581, 1411, 1328, 1220, 1145 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.49–8.52 (m, 1 H), 8.32 (s, 1 H), 8.05–8.07 (m, 1 H), 7.88 (d, *J* = 8.1 Hz, 2 H), 7.68 (ddd, *J* = 8.1, 7.20, 1.5 Hz, 1 H), 7.51 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1 H), 7.43 (dd, *J* = 9.8, 15.9 Hz, 1 H), 7.29 (d, *J* = 8.1 Hz, 2 H), 6.76 (d, *J* = 15.9 Hz, 1 H), 6.32–6.38 (m, 1 H), 6.10–6.17 (m, 1 H), 2.37 (s, 3 H), 2.22 (q, *J* = 5.6 Hz, 2 H), 1.33–1.49 (m, 4 H), 0.93 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 156.10, 149.57, 145.03, 144.91, 141.56, 137.22, 130.36, 130.15, 130.02, 129.80, 128.97, 127.88, 127.70, 124.08, 120.83, 119.74, 32.77, 31.18, 22.27, 21.59, 13.91.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{24}H_{25}KNO_2S$: 430.1243; found: 430.1241.

2-(Furan-2-yl)-4-tosylquinoline (8f)

Brown solid; yield: 71 mg (86%); mp 182–184 °C.

IR (KBr): 3424, 3137, 1589, 1496, 1317, 1161, 1141, 1084, 814, 660 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.62 (s, 1 H), 8.55–8.58 (m, 1 H), 8.16 (d, *J* = 8.4 Hz, 1 H), 7.91 (d, *J* = 8.1 Hz, 2 H), 7.67–7.74 (m, 2 H), 7.55 (ddd, *J* = 8.4, 7.10, 1.4 Hz, 1 H), 7.26–7.33 (m, 3 H), 6.62–6.64 (m, 1 H), 2.38 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 152.68, 149.48, 148.53, 145.82, 145.05, 144.96, 137.43, 130.65, 130.38, 130.08, 128.06, 127.98, 124.21, 120.95, 118.16, 112.65, 111.60, 21.61.

HRMS MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_3S$: 372.0670; found: 372.0670.

2-(2-Bromophenyl)-4-tosylquinoline (8g)

Brown solid; yield: 51 mg (70%); mp 172–174 °C.

IR (KBr): 3424, 3066, 2913, 1593, 1495, 1399, 1323, 1145, 1087, 810, 769 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.71–7.74 (m, 1 H), 8.51 (m, 1 H), 8.22–8.25 (m, 1 H), 7.94 (d, *J* = 8.3 Hz, 2 H), 7.79 (ddd, *J* = 8.4, 7.10, 1.5 Hz, 1 H), 7.66–7.74 (m, 3 H), 7.49 (ddd, *J* = 7.6, 7.1, 1.2 Hz, 1 H), 7.31–7.37 (m, 3 H), 2.39 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 158.12, 149.29, 145.13, 144.80, 140.20, 137.30, 133.49, 131.67, 130.77, 130.52, 130.12, 128.84, 128.14, 127.99, 124.22, 123.12, 121.86, 121.08, 21.64.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{22}H_{16}BrKNO_2S$: 475.9722; found: 475.9723.

7-Fluoro-2-phenyl-4-tosylquinoline (8i)

Yellow solid; yield: 65 mg (83%); mp 203–204 °C.

IR (KBr): 3430, 3084, 1618, 1587, 1508, 1453, 1325, 1150, 1082, 846, 680 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.63–8.67 (m, 2 H), 8.22–8.24 (dd, *J* = 1.8, 8.3 Hz, 2 H), 7.90 (d, *J* = 8.4 Hz, 2 H), 7.84 (dd, *J* = 9.6, 2.7 Hz, 1 H), 7.51–7.59 (m, 3 H), 7.36–7.41 (m, 1 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 2.39 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 163.35 (d, $^1J_{C-F}$ = 253 Hz), 157.97, 151.01 (d, $^2J_{C-F}$ = 13 Hz), 146.16, 146.15, 145.25, 137.75, 137.25, 130.58, 130.18, 129.15, 127.92, 127.65, 126.40 (d, $^3J_{C-F}$ = 9.6 Hz), 118.50 (d, $^3J_{C-F}$ = 2.4 Hz), 118.02 (d, $^4J_{C-F}$ = 1.2 Hz), 114.42 (d, $^2J_{C-F}$ = 20.1 Hz), 21.64.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{22}H_{16}FKNO_2S$: 416.0523; found: 416.0523.

2-(Naphthalen-1-yl)-4-tosylquinoline (8j)

Brown solid; yield: 66 mg (88%); mp 206–207 °C.

IR (KBr): 3424, 3054, 1585, 1493, 1318, 1138, 1085, 969, 784, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.74–8.76 (m, 1 H), 8.50 (s, 1 H), 8.27–8.30 (m, 1 H), 8.13–8.16 (m, 1 H), 7.93–8.01 (m, 4 H), 7.77–7.83 (m, 2 H), 7.69 (ddd, *J* = 8.5, 6.9, 1.3 Hz, 1 H), 7.63 (dd, *J* = 8.1, 1.2 Hz, 1 H), 7.51–5.57 (m, 2 H), 7.31–7.33 (m, 2 H), 2.38 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 158.99, 149.47, 145.65, 145.14, 137.38, 137.09, 134.09, 130.94, 130.82, 130.63, 130.15, 130.05, 128.64, 128.38, 128.08, 127.14, 126.30, 125.40, 125.14, 124.22, 123.32, 120.92, 21.64.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{26}H_{19}KNO_2S$: 448.0774; found: 448.0775.

2-(*m*-Tolyl)-4-tosylquinoline (8k)

White solid; yield: 71 mg (89%); mp 130–131 °C.

IR (KBr): 3424, 3046, 2917, 1593, 1580, 1322, 1145, 1085, 761 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.70 (s, 1 H), 8.59–8.61 (m, 1 H), 8.21–8.24 (m, 1 H), 8.01–8.07 (m, 2 H), 7.91 (d, *J* = 8.3 Hz, 2 H), 7.74 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1 H), 7.58 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1 H), 7.45 (t, *J* = 7.8 Hz, 1 H), 7.28–7.35 (m, 3 H), 2.50 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 156.98, 149.62, 145.75, 144.98, 138.86, 138.11, 137.56, 131.07, 130.78, 130.44, 130.06, 129.01, 128.21, 128.20, 127.93, 124.77, 124.08, 121.05, 119.42, 21.60, 21.56.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{23}H_{19}KNO_2S$: 412.0774; found: 412.0776.

2-(4-Methoxyphenyl)-4-tosylquinoline (8l)

White solid; yield: 67 mg (87%); mp 151–152 °C.

IR (KBr): 3424, 2996, 2929, 2834, 1606, 1589, 1495, 1400, 1322, 1252, 1150, 1085, 831, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 8.55–8.58 (m, 1 H), 8.16–8.24 (m, 3 H), 7.90 (d, *J* = 8.2 Hz, 2 H), 7.72 (ddd, *J* = 8.4, 7.10, 1.5 Hz, 1 H), 7.55 (ddd, *J* = 8.4, 7.10, 1.5 Hz, 1 H), 7.28–7.31 (m, 2 H), 7.08 (d, *J* = 8.6 Hz, 2 H), 3.91 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 161.59, 158.31, 149.65, 145.92, 144.93, 137.59, 130.72, 130.57, 130.38, 130.05, 129.05, 127.91, 127.80, 124.07, 120.73, 118.87, 114.50, 55.48, 21.61.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{23}H_{19}KNO_3S$: 428.0723; found: 428.0720.

2-(4-Chlorophenyl)-4-tosylquinoline (8m)

White solid; yield: 68 mg (91%); mp 187–188 °C.

IR (KBr): 3432, 3066, 1591, 1416, 1324, 1144, 1088, 836, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 8.59–8.91 (m, 1 H), 8.18–8.22 (m, 3 H), 7.90 (d, *J* = 8.4 Hz, 2 H), 7.76 (t, *J* = 8.1 Hz, 1 H), 7.60 (ddd, *J* = 8.5, 7.10, 1.4 Hz, 1 H), 7.54 (d, *J* = 8.4 Hz, 2 H), 7.31 (d, *J* = 8.1 Hz, 2 H), 2.38 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 155.49, 149.62, 146.12, 145.11, 137.48, 136.65, 136.56, 130.82, 130.66, 130.13, 129.33, 128.88, 128.49, 127.97, 124.15, 121.18, 118.81, 21.64.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{22}H_{16}ClKNO_2S$: 432.0227; found: 432.0226.

Methyl 3-(4-Tosylquinolin-2-yl)benzoate (8n)

White solid; yield: 62 mg (75%); mp 125–126 °C.

IR (KBr): 3424, 3075, 2954, 1931, 1716, 1579, 1494, 1399, 1294, 1151, 815, 770 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.9 (t, *J* = 1.9 Hz, 1 H), 8.75 (s, 1 H), 8.61–8.63 (m, 1 H), 8.46–8.49 (m, 1 H), 8.19–8.27 (m, 2 H), 7.92 (d, *J* = 8.2 Hz, 2 H), 7.78 ddd (*J* = 8.4, 7.10, 1.5 Hz, 1 H), 7.60–7.68 (m, 2 H), 7.32 (d, *J* = 8.2 Hz, 2 H), 4.01 (s, 3 H), 2.39 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.73, 155.66, 149.61, 146.16, 145.11, 138.50, 137.44, 131.93, 131.23, 131.17, 130.90, 130.66, 130.12, 127.27, 124.12, 121.26, 118.99, 52.38, 21.63.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{24}H_{19}KNO_4S$: 456.0672; found: 456.0672.

1-[4-(4-Tosylquinolin-2-yl)phenyl]ethan-1-one (8o)

White solid; yield: 58 mg (83%); mp 203–204 °C.

IR (KBr): 3332, 3050, 2929, 1682, 1586, 1493, 1420, 1325, 1151, 1086, 841, 765 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.73 (s, 1 H), 8.61–8.64 (m, 1 H), 8.35 (d, *J* = 8.1 Hz, 2 H), 8.23–8.26 (m, 1 H), 8.14 (d, *J* = 8.1 Hz, 2 H), 7.92 (d, *J* = 8.1 Hz, 2 H), 7.78 (ddd, *J* = 8.5, 7.10, 1.5 Hz, 1 H), 7.64 (ddd, *J* = 8.3, 7.10, 1.6 Hz, 1 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 2.69 (s, 3 H), 2.39 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 197.65, 155.39, 149.64, 146.21, 145.17, 142.15, 138.11, 137.38, 131.00, 130.75, 130.14, 129.02, 128.84, 127.98, 127.76, 124.16, 121.38, 119.13, 26.83, 21.63.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{24}H_{19}KNO_3S$: 440.0723; found: 440.0724.

4-Tosyl-2-[3-(trifluoromethyl)phenyl]quinoline (8p)

Yellow solid; yield: 68 mg (92%); mp 158–159 °C.

IR (KBr): 3428, 3071, 1594, 1434, 1321, 1237, 1150, 860, 766 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1 H), 8.61–8.64 (m, 1 H), 8.54 (s, 1 H), 8.42 (d, *J* = 7.9 Hz, 1 H), 8.24–8.27 (m, 1 H,), 7.92 (d, *J* = 8.3 Hz, 2 H), 7.79 (ddd, *J* = 8.5, 7.1, 1.4 Hz, 2 H), 7.70 (t, *J* = 7.9 Hz, 1 H), 7.64 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 2.39 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 155.05, 149.62, 146.39, 145.20, 138.91, 137.38, 131.63 (q, $^2J_{C-F}$ = 32.6 Hz), 130.96, 130.81, 130.71 (q, $^4J_{C-F}$ = 1.3 Hz), 130.16, 129.60, 128.82, 128.00, 126.78 (q, $^3J_{C-F}$ = 3.7 Hz), 124.06 (q, $^1J_{C-F}$ = 273 Hz), 124.48 (q, $^3J_{C-F}$ = 3.7 Hz), 124.17, 121.38, 118.77, 21.64.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{23}H_{16}F_3KNO_2S$: 466.0491; found: 466.0492.

2-(Thiophen-2-yl)-4-tosylquinoline (8q)

Brown solid; yield: 62 mg (78%); mp 191–192 °C.

IR (KBr): 3424, 3099, 3071, 1585, 1424, 1317, 1141, 1085, 816, 712 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 8.51–8.54 (m, 1 H), 8.11–8.13 (m, 1 H), 7.90 (d, *J* = 8.3 Hz, 2 H), 7.85–7.86 (m, 1 H), 7.70 (ddd, *J* = 8.4, 7.10, 1.4 Hz, 1 H), 7.51–7.56 (m, 2 H), 7.30 (d, *J* = 8.3 Hz, 2 H), 7.18–7.21 (m, 1 H), 2.38 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): 151.94, 149.42, 145.65, 145.07, 144.05, 137.38, 130.62, 130.27, 130.08, 129.92, 128.43, 127.93, 127.23, 124.14, 120.96, 118.18, 21.62.

HRMS MALDI-TOF: *m*/*z* [M + K]$^+$ calcd for $C_{20}H_{15}KNO_2S_2$: 404.0181; found: 404.0179.

4-Amino-2-phenylquinoline (9a); Typical Procedure for the Synthesis of 4-Aminoquinolines 9

A mixture of 2-phenyl-4-nitroquinoline (**7a**, 50 mg, 0.20 mmol), Pd/C (10 mg), and ammonium formate (63 mg, 1.0 mmol) in MeOH (2.5 mL) was stirred at r.t. for 4 h. Pd/C was filtered off through a short path of silica gel. The filtrate was extracted with water and EtOAc (3 ×). Evaporation of solvent followed by column chromatography (petroleum ether/EtOAc, 60:40) afforded **9a**; yield: 39 mg (89%).

2-(Furan-2-yl)quinolin-4-amine (9f)

Brown solid; yield: 28 mg (66%); mp 92–94 °C.

IR (KBr): 3478, 3299, 3058, 1645, 1595, 1516, 1216, 1013, 896, 751 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.03–8.05 (m, 1 H), 7.70–7.73 (m, 1 H), 7.64 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1 H), 7.57 (dd, *J* = 0.9, 1.8 Hz, 1 H), 7.38–7.42 (m, 1 H), 7.14 (dd, *J* = 0.8, 3.4 Hz, 1 H), 7.06 (s, 1 H), 6.55 (dd, *J* = 1.7, 3.4 Hz, 1 H), 4.79 (s, 2 H, NH_2).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 154.01, 149.97, 149.52, 148.94, 143.54, 129.84, 129.77, 124.81, 120.01, 118.08, 112.02, 109.03, 99.57.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{11}N_2O$: 211.0871; found: 211.0869.

1-[4-(4-Aminoquinolin-2-yl)phenyl]ethan-1-one (9o)

Yellow solid; yield: 22 mg (90%); mp 199–200 °C.

IR (KBr): 3465, 3054, 2921, 1682, 1578, 1399, 1266, 826, 757 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.01–8.05 (m, 5 H), 8.82 (d, *J* = 8.3 Hz, 1 H), 7.64–7.68 (m, 1 H), 7.42–7.46 (m, 1 H), 7.00 (d, *J* = 1.9 Hz, 1 H), 2.64 (s, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 198.41, 158.16, 151.63, 147.75, 143.74, 137.12, 130.32, 128.62, 127.71, 125.14, 120.51, 117.61, 101.49, 26.66

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{15}N_2O$: 263.1184; found: 263.1184.

2-Phenylquinolin-4(1*H*)-one (10a); Typical Procedure for the Synthesis of 2-Aryl-4-quinolones 10

This transformation was carried out according to ref. 13. A solution of 4-nitro-2-phenylquinoline (**7a**, 50 mg, 0.2 mmol) in TFA (1.4 mL) and 1.0 M H_2SO_4 (1.5 mL) was stirred at 50 °C for 4 h. After cooling to r.t., TFA was removed under reduced pressure. The mixture was extracted with sat. $NaHCO_3$ and EtOAc (3 ×). The combined organic phases were dried (Na_2SO4), and the solvent was removed under reduced pressure. The crude product was washed with Et_2O to give **10a**; yield: 41 mg (93%).

***N*,*N*-Dimethyl-2-pentylquinolin-4-amine (11c); Typical Procedure for the Synthesis of 4-(Dimethylamino)quinolines 11**

A mixture of 1-(2-aminophenyl)oct-1-yn-3-one (**2c**, 50 mg, 0.23 mmol) and 1.25 M NaOH solution (0.37 mL) in DMF (0.8 mL) and water (0.2 mL) was stirred at 60 °C for 1 h. After completion of reaction, the mixture was extracted with water and EtOAc (3 ×). The combined organic phases were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/EtOAc, 90:10) to give **11c** as a brown semisolid; yield: 24 mg (43%).

IR (neat): 3389, 3062, 2958, 2858, 1719, 1657, 1591, 1512, 1420, 1204, 1054, 851, 767 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.97–8.02 (m, 2 H), 7.60 (t, *J* = 7.8 Hz, 1 H), 7.40 (t, *J* = 7.8 Hz, 1 H), 6.67 (s, 1 H), 3.02 (s, 6 H), 2.87 (t, *J* = 8.0 Hz, 2 H), 1.78–1.84 (m, 2 H), 1.35–1.45 (m, 4 H), 0.91 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 163.29, 157.71, 149.44, 129.24, 128.74, 124.19, 123.90, 121.72, 107.39, 43.95, 39.75, 31.93, 29.99, 22.63, 14.09.

HRMS MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{23}N_2$: 243.1861; found: 243.1861.

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Supporting Information

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