Microwave-Promoted Alkynylation–Cyclization of 2-Aminoaryl Ketones: A Green Strategy for the Synthesis of 2,4-Disubstituted Quinolines

Iraj Mohammadpoor-Baltork,* Shahram Tangestaninejad,* Majid Moghadam, Valiollah Mirkhani, Salma Anvar, Arsalan Mirjafari

Catalysis Division, Department of Chemistry, University of Isfahan, Isfahan 81746-73441, Iran
Fax +98(311)6689732; E-mail: imbaltork@sci.ui.ac.ir; E-mail: stanges@sci.ui.ac.ir

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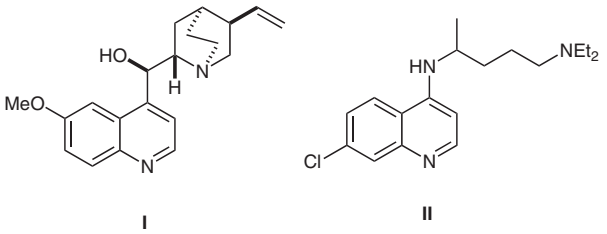
Abstract: A series of 2,4-disubstituted quinolines were easily prepared through a one-pot reaction of structurally diverse 2-aminoaryl ketones with various arylacetylenes in the presence of $K_5CoW_{12}O_{40}\cdot 3H_2O$ as a reusable and environmentally benign catalyst under microwave irradiation and solvent-free conditions.

Key words: 2,4-disubstituted quinolines, $K_5CoW_{12}O_{40}\cdot 3H_2O$, microwave irradiation, 2-aminoaryl ketones, arylacetylenes

Quinoline and, more specifically, substituted quinolines exist in many natural products and have a wide spectrum of biological activities.[1] They have proven to be key compounds for the synthesis of therapeutic agents e.g., antimicrobial, antibacterial, antiinflammatory, antiplatelet and antimalarials.[2] Known substituted quinoline drugs are quinine **I**, which is used as an antipyretic (fever-reducing), and chloroquine **II**, which is an antimalarial drug[3] (Figure 1). Besides pharmacological activity, compounds containing the 4-arylquinoline substructure have found many applications, for example, as chemosensors for fluoride ions,[4] and as fluorescent sensors for the detection of metal ions in aqueous solutions.[5] Various cyclization processes leading to these heterocycles, have been reported in the literature, for example, Skraup,[6] Doebner and Miller,[7] Friedländer,[8] Combes,[9] and others.[10] Recently, the synthesis of substituted quinolines has been reported to take place by Meyer–Schuster rearrangement of 2-aminoaryl ketones and phenylacetylene in the presence of $In(OTf)_3$ and $Zn(OTf)_2$/[hmim]PF_6.[11] However, in spite of their potential utility, some of the reported methods involve the use of Lewis or Brønsted acids. These traditional acids are corrosive and produce significant amounts of waste, which limit their usefulness and cause serious environmental and safety concerns. Furthermore, long reaction times, low yields, tedious work-up, formation of by products, and the use of expensive reagents and toxic organic solvents, are other disadvantages of some of these methods. Due to their importance and useful properties, the development of an efficient, general and environmentally benign method for the preparation of these widely used heterocyclic compounds is a major challenge in synthetic organic chemistry. Consequently, a method that uses $K_5CoW_{12}O_{40}\cdot 3H_2O$ catalyst should greatly contribute to the development of green processes. To the best of our knowledge, there are no reports on the use of $K_5CoW_{12}O_{40}\cdot 3H_2O$ as a heterogeneous catalyst for the synthesis of substituted quinolines.



I II

Figure 1 Structure of quinine (**I**) and chloroquine (**II**); two quinoline-based drugs

The high catalytic activity of heteropoly compounds has received significant interest in recent years.[12] Because of their weak super-acidic and redox properties, low toxicity, ease of handling, low cost, stability, recoverability, and reusability, heteropoly compounds have been used as versatile heterogeneous and environmentally friendly catalysts in different areas of organic synthesis. The $[Co^{III}W_{12}]^{5-}$ anion is a well-defined outer-sphere electron-transfer agent.[13] During the intervening time, the potential utility of numerous POM anions as electron-transfer agents in the selective catalytic oxidations of inorganic and organic substrates of practical importance has been recognized.[14] Due to the successful applications of $K_5CoW_{12}O_{40}\cdot 3H_2O$ as a catalyst, several synthetically useful organic transformations using this salt have been reported in the literature.[15]

As a part of our ongoing program to develop practical and eco-friendly synthetic methodologies,[16] we wish to report a novel and straightforward synthesis of substituted quinolines via a one-pot reaction of 2-aminoaryl ketones and arylacetylenes in the presence of $K_5CoW_{12}O_{40}\cdot 3H_2O$ as a reusable catalyst under microwave irradiation and solvent-free conditions (Scheme 1).

Initially, 2-aminobenzophenone and phenylacetylene were chosen as model substrates for optimization of the reaction conditions (Table 1). The reaction of 2-aminobenzophenone (1 mmol) and phenylacetylene (1 mmol) was first performed in the absence of the catalyst under microwave irradiation[17] (1000 W) at 110 °C in order to establish the effectiveness of the catalyst. Under

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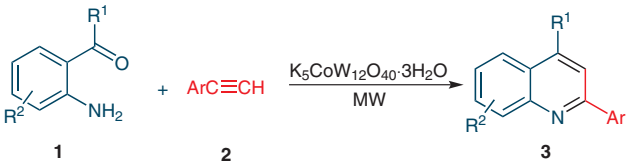


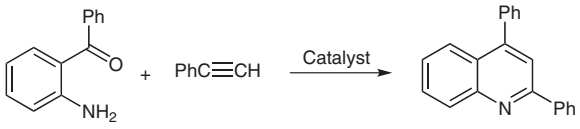
1 2 3

Scheme 1 Microwave-promoted synthesis of 2,4-disubstituted quinolines **3** by the reaction of 2-aminoaryl ketones **1** and arylacetylenes **2** catalyzed by $K_5CoW_{12}O_{40}·3H_2O$

these conditions, the reaction did not proceed and the starting materials remained intact in the reaction mixture (Table 1, entry 1). Then, the same reaction was examined in the presence of different heteropoly compounds (10 mol%) as catalysts for 15 minutes (Table 1, entries 2–7). The results revealed that $K_5CoW_{12}O_{40}·3H_2O$ was the most effective catalyst in this reaction (Table 1, entry 7). Next, we tested the effect of reaction time, the amount of catalyst, the temperature and the MW power on the yield of the product. Increasing either the temperature or the amount of catalyst and/or prolonging the reaction time did not improve the yield (Table 1, entries 8–10), while reducing these parameters or reducing the microwave power led to a reduction in product yield (Table 1, entries 11–14). In order to ascertain the effectiveness of microwave heating, the reaction was also conducted using conventional heating (110 °C) and the desired product was obtained in only 15% yield after 3 hours (Table 1, entry 15). Therefore, 1:1:0.01 molar ratios of 2-aminobenzophenone, phenylacetylene and $K_5CoW_{12}O_{40}·3H_2O$ and a power of 1000 W at 110 °C were found to be the optimal conditions.

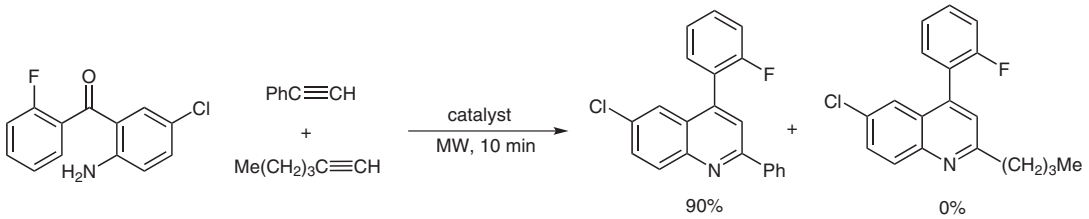
A series of reactions were carried out to study the scope and generality of the catalyst under the optimum conditions. A wide range of substituted and structurally diverse 2-aminoaryl ketones and arylacetylenes were used, and the corresponding 2,4-diaryl quinolines were synthesized in excellent yields (Table 2, entries 1–18).[18] 2-Aminoacetophenone as an alkyl substituted ketone was also converted efficiently into its corresponding quinoline in the presence of this catalyst (Table 2, entries 19 and 20). The reaction was generally clean and no side products, such as dihydroquinolines, were produced; in all cases, 2,4-disubstituted quinolines were obtained as the sole products. As shown in Table 2, the presence of electron-withdrawing or electron-donating substituents on the aromatic rings of starting materials had no significant effect on the yields of the products. It is noteworthy that alkylacetylenes, such as 1-hexyne, did not afford the corresponding quinoline under the same reaction conditions. These results indicate that the present protocol is potentially applicable to the chemoselective conversion of arylacetylenes into their quinolines in the presence of alkylacetylenes. In this manner, the reaction of an equimolar mixture of phenylacetylene and 1-hexyne with 2-amino-5-chloro-2′-fluorobenzophenone (Table 1, entry 4) was performed under microwave irradiation. It was observed that only phenylacetylene reacted and that 1-hexyne remained intact in the reaction mixture (Scheme 2).

Table 1 Optimization of the Reaction Conditions for the Synthesis of 2,4-Diphenylquinoline (**3a**)[a]



Entry	Catalyst (mol%)	Temp (°C)	Time (min)	Yield (%)[b]
1	no catalyst	110	15	0
2	$H_3PW_{12}O_{40}$ (10)	110	15	65
3	$H_3PMo_{12}O_{40}$ (10)	110	15	46
4	$H_4SiW_{12}O_{40}$ (10)	110	15	43
5	$AlPW_{12}O_{40}$ (10)	110	15	32
6	$AlPMo_{12}O_{40}$ (10)	110	15	40
7	$K_5CoW_{12}O_{40}·3H_2O$ (10)	110	15	95
8	$K_5CoW_{12}O_{40}·3H_2O$ (10)	120	15	95
9	$K_5CoW_{12}O_{40}·3H_2O$ (12)	110	15	95
10	$K_5CoW_{12}O_{40}·3H_2O$ (10)	110	20	95
11	$K_5CoW_{12}O_{40}·3H_2O$ (10)	100	15	80
12	$K_5CoW_{12}O_{40}·3H_2O$ (8)	110	15	70
13	$K_5CoW_{12}O_{40}·3H_2O$ (10)	110	10	81
14[c]	$K_5CoW_{12}O_{40}·3H_2O$ (10)	110	15	70
15[d]	$K_5CoW_{12}O_{40}·3H_2O$ (10)	110	180	15

[a] Reaction conditions: 2-aminobenzophenone (1 mmol), phenylacetylene (1 mmol), applied power of 1000 W.
[b] Isolated yield.
[c] Reaction was performed with applied power of 800 W.
[d] Reaction was performed under thermal conditions.



Scheme 2 Selective conversion of arylacetylene into the corresponding quinoline in the presence of alkylacetylene catalyzed by $K_5CoW_{12}O_{40}·3H_2O$

Table 2 Microwave-Promoted Synthesis of 2,4-Disubstituted Quinolines Catalyzed by $K_5CoW_{12}O_{40}·3H_2O$[a]

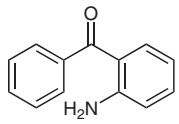
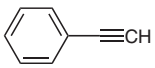
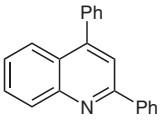
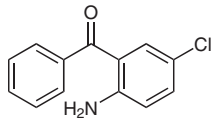
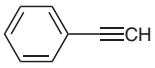
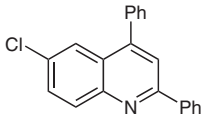
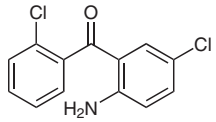
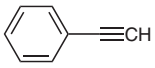
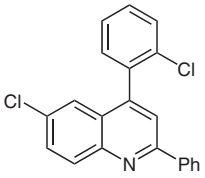
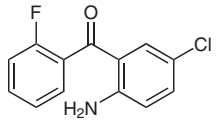
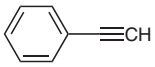
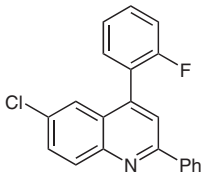
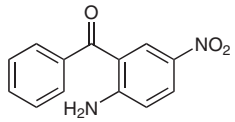
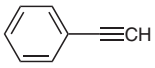
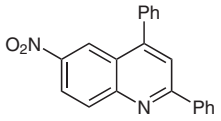
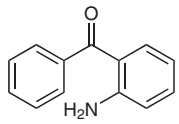
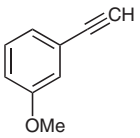
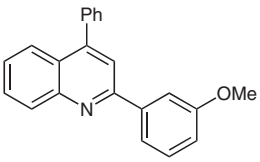
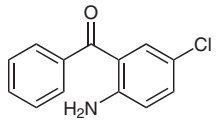
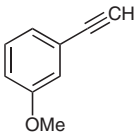
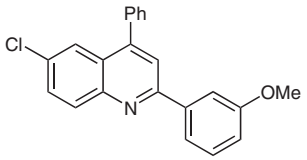
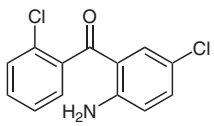
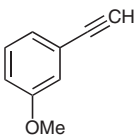
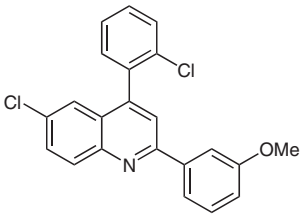
Entry	2-Aminoaryl ketone	Acetylene	Quinoline	Time (min)	Yield (%)[b]
1			 **3a**	15	95
2			 **3b**	15	95
3			 **3c**	10	96
4			 **3d**	10	90
5			 **3e**	10	90
6			 **3f**	15	84
7			 **3g**	20	84
8			 **3h**	10	89

Table 2 Microwave-Promoted Synthesis of 2,4-Disubstituted Quinolines Catalyzed by $K_5CoW_{12}O_{40}·3H_2O$[a] (continued)

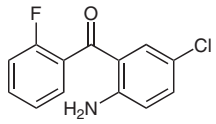
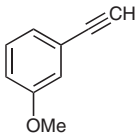
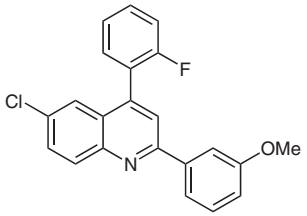
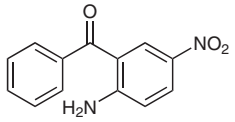
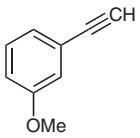
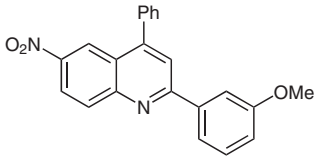
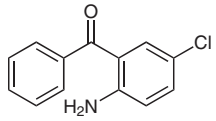
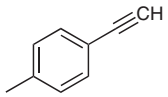
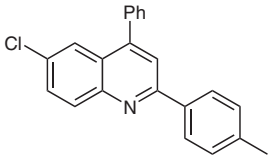
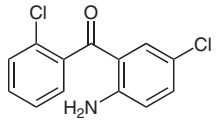
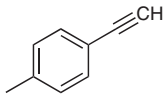
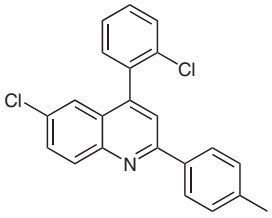
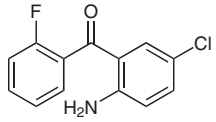
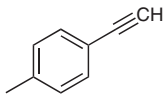
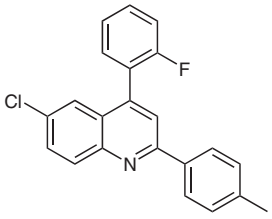
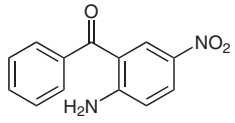
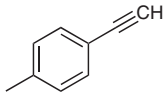
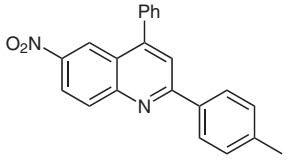
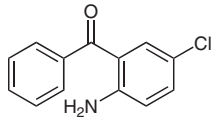
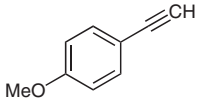
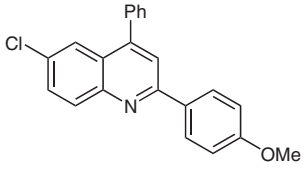
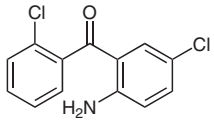
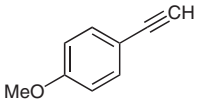
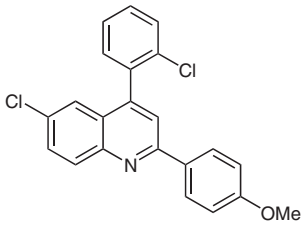
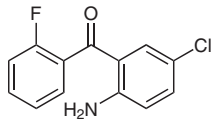
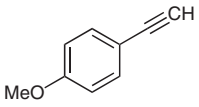
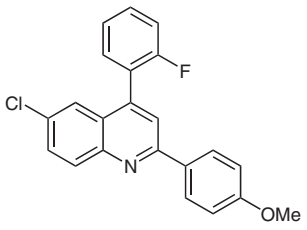
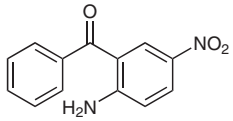
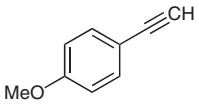
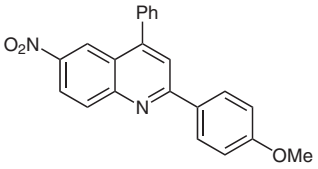
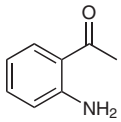
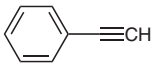
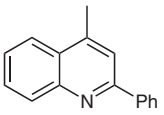
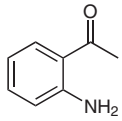
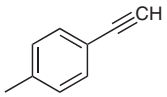
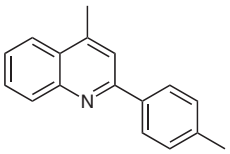
Entry	2-Aminoaryl ketone	Acetylene	Quinoline	Time (min)	Yield (%)[b]
9			 **3i**	10	90
10			 **3j**	15	90
11			 **3k**	5	90
12			 **3l**	15	93
13			 **3m**	5	96
14			 **3n**	5	95
15			 **3o**	10	96

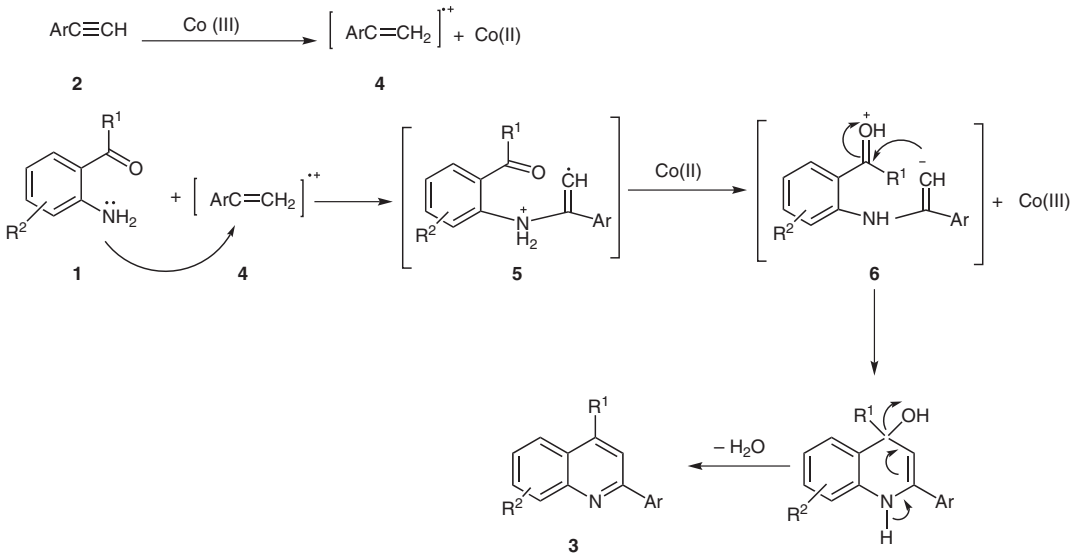
Table 2 Microwave-Promoted Synthesis of 2,4-Disubstituted Quinolines Catalyzed by $K_5CoW_{12}O_{40}·3H_2O$[a] (continued)

Entry	2-Aminoaryl ketone	Acetylene	Quinoline	Time (min)	Yield (%)[b]
16			 **3p**	15	84
17			 **3q**	15	86
18			 **3r**	10	90
19			 **3s**	20	75
20			 **3t**	20	82

[a] Reaction conditions: 2-Aminoaryl ketone (1 mmol), arylacetylene (1 mmol), catalyst (10 mol%) and 1000 W microwave power at 110 °C.
[b] Isolated yield.

The structure of the products was deduced from their IR, mass, ^1H and ^{13}C NMR spectra and by their elemental analysis. Furthermore, the structure of **3h** was confirmed by X-ray crystallographic analysis (CCDC 781894, Figure 2).

The actual mechanism of the reaction is not clear at present. However, according to published results,[13,14] the mechanism can be explained on the basis of an electron-transfer phenomenon, in which the arylacetylene **2** is first oxidized to a radical-cation intermediate **4** by transferring an electron to Co(III) to produce Co(II). Nucleophilic attack of 2-aminoaryl ketone **1** on **4** affords **5**. One electron transfer from Co(II) to **5** gives **6** and regenerates the Co(III) species, which enters the next catalytic cycle. Finally, cyclization of **6** followed by elimination of water affords the desired product **3** (Scheme 3). To validate the suggested mechanism, a radical scavenger such as acrylamide was added to the reaction mixture. Under these conditions, after exposing the mixture to MW irradiation, no progress was observed in the reaction, which is a good indication of the presence of radical species in the reaction. Another reasonable explanation for the mechanism is that the water reacts with radical cation **4** and produces the acetophenone, which then reacts with 2-aminoaryl ketone **1** to afford the desired product. On the basis of this reasoning, the reaction can occur via two paths and therefore the reaction must be accelerated. In this manner, the reaction of phenylacetylene with catalyst was investigated in the absence of 2-aminoaryl ketone **1** and it was found that, under these conditions, less than 5% of acetophene was produced. When the model reaction was carried out in the presence of water, only 30% of 2,4-disubstituted quinoline was obtained. Therefore, the addition of water deactivates the catalyst and decreases the yield. All these



Scheme 3 Proposed mechanism for $K_5CoW_{12}O_{40}·3H_2O$ catalyzed synthesis of 2,4-disubstituted quinolines

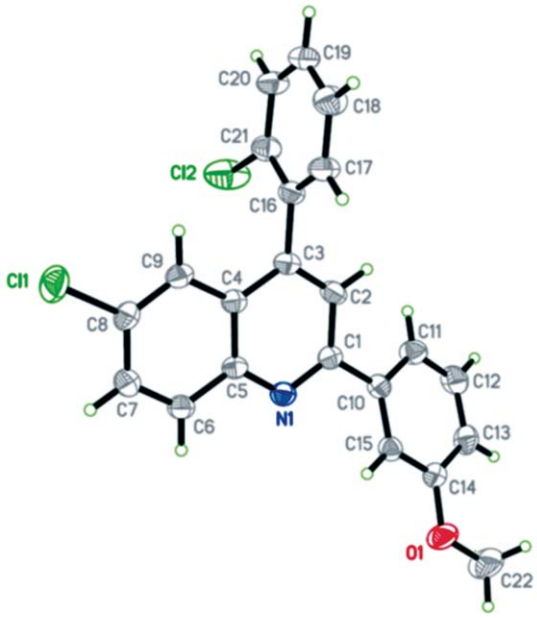


Figure 2 X-ray crystal structure of **3h**

observations showed that the proposed mechanism (Scheme 3) is more reasonable.

The reusability and recycling of the $K_5CoW_{12}O_{40}·3H_2O$ catalyst, which is one of the key advantages of this procedure, was tested in the reaction of 2-aminobenzophenone and phenylacetylene as a model. After completion of the reaction, the mixture was cooled to room temperature; the catalyst was separated by simple filtration by diluting with cold ethanol and dried at 100 °C. The recovered catalyst could be reused at least five additional times in subsequent reactions without significant loss of activity (Table 3).

In conclusion, we have reported an efficient, microwave-promoted, one-pot synthesis of 2,4-disubstituted quinolines via cyclocondensation of 2-aminoaryl ketones and arylacetylenes using a sub-stoichiometric amount of $K_5CoW_{12}O_{40}·3H_2O$ under solvent-free conditions. The notable features of this method are simple operation, environmentally friendly experimental conditions, short reaction times and high yields of isolated products. In addition, easy recovery and reuse of the catalyst and the avoidance of toxic organic solvents make this procedure an economical and green process for the synthesis of quinoline derivatives.

Table 3 Reuse of $K_5CoW_{12}O_{40}·3H_2O$ Catalyst for the Synthesis of **3a**[a]

Run	Cycle	Yield (%)[b]
1	0	95
2	1	95
3	2	92
4	3	90
5	4	87
6	5	85

[a] Reaction conditions: 2-Aminobenzophenone (1 mmol), phenylacetylene (1 mmol), catalyst (10 mol%), 1000 W microwave power at 110 °C, 15 min.
[b] Isolated yield.

Acknowledgment

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(17) The microwave system used in these experiments includes the following items: Micro-SYNTH labstation, equipped with a glass door, a dual magnetron system with pyramid-shaped diffuser, 1000 W delivered power, exhaust system, magnetic stirrer, 'quality pressure' sensor for flammable organic solvents, and a ATCFO fiber optic system for automatic temperature control
(18) **Synthesis of 2,4-Disubstituted Quinolines; General Procedure**
A mixture of 2-aminoaryl ketone **1** (1 mmol), arylacetylene **2** (1 mmol) and $K_5WCo_{12}O_{40}\cdot 3H_2O$ (10 mol%) was irradiated under solvent-free conditions for the appropriate time (Table 2). The progress of the reaction was monitored by TLC (*n*-hexane–EtOAc, 9:1). After completion of the reaction, the mixture was cooled to r.t. and cold EtOH (20 mL) was added. The residue was filtered, the filtrate was evaporated, and the crude product was purified by recrystallization from EtOH to afford the pure product in 75–96% yields.
2,4-Diphenylquinoline (3a)
Mp 107–109 °C (Lit.[11b] 107 °C). IR (KBr): 3062, 2922, 1616, 1475, 1317, 1274, 960, 767 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.45 (m, 2 H), 7.47–7.55 (m, 7 H), 7.70 (t, *J* = 7.5 Hz, 1 H), 7.77 (s, 1 H), 7.88 (d, *J* = 3.2 Hz, 1 H), 8.15 (d, *J* = 8.1 Hz, 2 H), 8.21 (d, *J* = 8.8 Hz, 1 H). MS: *m*/*z* = 281.09 (7.07) $[M]^+$, 254.15 (91.45), 179.41 (21.88), 103.16 (35.60), 77.18 (100.00), 51.23 (33.55).
6-Chloro-2,4-diphenylquinoline (3b)
Mp 98–99 °C (Lit.[10g] 98 °C). IR (KBr): 2922, 2852, 1587, 1543, 1481, 887, 823, 779, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.50 (m, 1 H), 7.53–7.60 (m, 7 H), 7.68 (dd, ^1J = 9.0 Hz, ^2J = 2.2 Hz, 1 H), 7.85 (s, 1 H), 7.87 (d, *J* = 2.0 Hz, 1 H), 8.17–8.20 (m, 3 H). MS: *m*/*z* = 317.08 (2.15) $[M + 2]^+$, 315.03 (8.10) $[M]^+$, 280.11 (6.22), 238.08 (2.63), 103.05 (20.24), 77.05 (100.00), 51.09 (57.09).
6-Chloro-4-(2-chlorophenyl)-2-phenylquinoline (3c)
Mp 112–114 °C (Lit.[11b] 112 °C). IR (KBr): 2951, 1643, 1469, 1365, 1228, 1022, 829 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.41 (m, 1 H), 7.44–7.50 (m, 4 H), 7.53–7.56 (m, 2 H), 7.62 (d, *J* = 7.9 Hz, 1 H), 7.67 (dd, ^1J = 9.0 Hz, ^2J = 2.1 Hz, 1 H), 7.84 (s, 1 H), 8.19–8.21 (m, 3 H). MS: *m*/*z* = 351.02 (11.13) $[M + 2]^+$, 349.00 (17.97) $[M]^+$, 314.06 (5.91), 279.12 (13.09), 278.13 (38.28), 201.10 (22.46), 102.96 (38.87), 76.96 (81.25), 74.97 (50.78), 50.98 (100.00).
6-Chloro-4-(2′-fluorophenyl)-2-phenylquinoline (3d)
Mp 124–126 °C (Lit.[11b] 125 °C). IR (KBr): 3055, 2922, 2850, 1593, 1544, 1481, 1354, 885, 835, 802, 756 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.37 (m, 2 H), 7.44–7.56 (m, 5 H), 7.66–7.70 (m, 2 H), 7.88 (s, 1 H), 8.19 (d, *J* = 8.2 Hz, 3 H). MS: *m*/*z* = 334.02 (8.59) $[M + 2]^+$, 331.98

(21.56) [M]$^+$, 298.08 (6.33), 194.07 (14.61), 102.96 (49.38), 76.96 (100.00), 74.95 (65.63), 50.97 (96.25).

2,4-Diphenyl-6-nitroquinoline (3e)

Mp 265–266 °C (Lit.[10h] 264 °C). IR (KBr): 2922, 2852, 1595, 1440, 1382, 1338, 883, 846, 771, 752 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = **7**.54–7.64 (m, 8 H), 7.99 (s, 1 H), 8.26 (d, *J* = 7.0 Hz, 2 H), 8.35 (d, *J* = 9.2 Hz, 1 H), 8.50 (dd, ^1J = 9.2 Hz, ^2J = 2.4 Hz, 1 H), 8.87 (d, *J* = 2.4 Hz, 1 H). MS: *m*/*z* = 326.11 (3.20) [M]$^+$, 244.02 (13.24), 203.06 (10.96), 146.58 (27.40), 100.66 (25.11), 78.08 (29.68), 77.04 (81.28), 55.10 (100.00).

2-(3-Methoxyphenyl)-4-phenylquinoline (3f)

Mp 170 °C. IR (KBr): 2922, 2852, 1625, 1544, 1462, 1097 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.94 (s, 3 H), 7.04 (d, *J* = 7.1 Hz, 1 H), 7.44 (t, *J* = 8.3 Hz, 1 H), 7.49–7.58 (m, 6 H), 7.73–7.78 (m, 2 H), 7.80–7.82 (m, 2 H), 7.92 (d, *J* = 8.5 Hz, 1 H), 8.28 (s, 1 H). MS: *m*/*z* = 311.06 (26.34) [M]$^+$, 310.03 (35.61), 281.06 (15.85), 267.10 (4.70), 241.04 (5.03), 204.08 (9.88), 176.04 (21.59), 140.08 (16.95), 57.05 (92.20), 55.05 (100.00).

6-Chloro-2-(3-methoxyphenyl)-4-phenylquinoline (3g)

Mp 129–130 °C. IR (KBr): 2924, 2831, 1600, 1543, 1485, 1344, 1041, 877, 823, 769 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.94 (s, 3 H, OMe), 7.04 (dd, ^1J = 8.2 Hz, ^2J = 2.4 Hz, 1 H), 7.44 (t, *J* = 8.0 Hz, 1 H), 7.54–7.60 (m, 5 H), 7.67 (dd, ^1J = 8.2 Hz, ^2J = 2.3 Hz, 1 H), 7.73 (d, *J* = 7.6 Hz, 1 H), 7.79 (s, 1 H), 7.83 (s, 1 H), 7.87 (d, *J* = 1.7 Hz, 1 H), 8.18 (d, *J* = 8.9 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.47, 112.72, 115.70, 120.01, 120.14, 124.51, 126.60, 128.75, 128.86, 129.49, 129.90, 130.47, 131.78, 132.29, 137.77, 140.68, 147.19, 148.44, 156.86, 160.23. MS: *m*/*z* = 347.98 (5.99) [M + 2]$^+$, 345.99 (48.98) [M]$^+$, 343.98 (100.00), 317.99 (6.51), 314.99 (27.87), 203.11 (14.34), 155.01 (21.52), 139.04 (23.57), 132.55 (27.66), 77.13 (7.68). Anal. Calcd for $C_{22}H_{16}ClNO$ (345.09): C, 76.41; H, 4.66; N, 4.05. Found: C, 76.28; H, 4.71; N, 3.97.

6-Chloro-4-(2-chlorophenyl)-2-(3-methoxyphenyl)-quinoline (3h)

Mp 168–169 °C. IR (KBr): 2922, 2850, 1604, 1583, 1544, 1471, 1433, 1282, 1174, 1043, 887, 839, 763, 705 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.94 (s, 3 H), 7.04 (dd, ^1J = 8.2 Hz, ^2J = 2.5 Hz, 1 H), 7.39 (dd, ^1J = 7.4 Hz, ^2J = 1.7 Hz, 1 H), 7.42–7.51 (m, 4 H), 7.61 (d, *J* = 9.0 Hz, 1 H), 7.67 (dd, ^1J = 7.8 Hz, ^2J = 2.2 Hz, 1 H), 7.72 (d, *J* = 7.6 Hz, 1 H), 7.79–7.81 (m, 2 H), 8.18 (d, *J* = 9.0 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.48, 112.73, 115.81, 120.03, 120.70, 124.41, 126.65, 127.04, 129.91, 130.12, 130.17, 130.65, 131.37, 131.76, 132.45, 133.34, 136.34, 140.51, 145.78, 146.90, 156.81, 160.26. MS: *m*/*z* = 383.12 (8.09) [M + 4]$^+$, 381.14 (4.30) [M + 2]$^+$, 379.00 (72.32) [M]$^+$, 378.14 (100.00), 350.11 (27.90), 237.12 (15.63), 132.85 (22.99), 75.06 (20.09). Anal. Calcd for $C_{22}H_{15}Cl_2NO$ (379.05): C, 69.49; H, 3.98; N, 3.68. Found: C, 69.32; H, 4.03; N, 3.75.

6-Chloro-4-(2-fluorophenyl)-2-(3-methoxyphenyl)-quinoline (3i)

Mp 114–115 °C. IR (KBr): 3035, 2935, 2835, 1589, 1544, 1483, 1280, 1043, 887, 761 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.94 (s, 3 H), 7.04 (dd, ^1J = 8.1 Hz, ^2J = 2.4 Hz, 1 H), 7.30 (t, *J* = 9.0 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 1 H), 7.42–7.47 (m, 2 H), 7.53–755 (m, 1 H), 7.65 (s, 1 H), 7.68 (dd, ^1J = 8.9 Hz, ^2J = 2.2 Hz, 1 H), 7.72 (d, *J* = 7.7 Hz, 1 H), 7.79 (s, 1 H), 7.86 (s, 1 H), 8.19 (d, *J* = 8.9 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.47, 112.74, 115.75, 116.20, 116.37, 120.01, 121.06, 124.37, 124.59, 125.08, 125.21, 126.72, 129.89, 130.62, 130.85, 130.91, 131.63, 131.65, 131.77, 132.48, 140.54, 142.53, 146.97, 156.84, 158.67, 160.25, 160.65. MS: *m*/*z* = 365.15 (44.01) [M + 2]$^+$, 363.15 (93.39) [M]$^+$, 362.15 (100.00), 334.14 (52.69), 333.14 (60.33), 332.12 (44.01), 296.13 (16.53), 283.13 (15.91), 141.59 (23.35), 99.04 (8.01), 51.10 (5.58). Anal. Calcd for $C_{22}H_{15}ClFN$ (347.09): C, 72.63; H, 4.16; N, 3.85. Found: C, 72.51; H, 4.21; N, 3.78.

2-(3-Methoxyphenyl)-6-nitro-4-phenylquinoline (3j)

Mp 194–195 °C. IR (KBr): 2922, 2852, 1620, 1597, 1554, 1340, 1267, 1035, 875, 810, 702 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.95 (s, 3 H), 7.08 (dd, ^1J = 8.17 Hz, ^2J = 2.0 Hz, 1 H), 7.47 (t, *J* = 8.0 Hz, 1 H), 7.57–7.64 (m, 5 H), 7.79 (d, *J* = 7.7 Hz, 1 H), 7.85 (s, 1 H), 7.97 (s, 1 H), 8.34 (d, *J* = 9.3 Hz, 1 H), 8.50 (dd, ^1J = 8.8 Hz, ^2J = 1.8 Hz, 1 H), 8.86 (d, *J* = 2.1 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.51, 113.07, 116.47, 120.27, 120.83, 122.91, 123.08, 124.93, 129.16, 129.35, 129.47, 130.04, 131.82, 136.92, 139.98, 145.49, 151.02, 151.27, 159.83, 160.33. MS: *m*/*z* = 356.13 (85.19) [M]$^+$, 355.11 (100.00), 326.08 (14.89), 241.16 (19.52), 201.16 (25.31), 176.20 (29.32), 139.27 (32.10), 132.61 (31.48), 78.11 (26.85), 77.10 (91.36), 51.13 (51.23). Anal. Calcd for $C_{22}H_{16}N_2O$ (324.13): C, 74.15; H, 4.53; N, 7.86. Found: C, 73.97; H, 4.57; N, 7.92.

6-Chloro-4-phenyl-2-*p*-tolylquinoline (3k)

Mp 123–124 °C (Lit.[10i] 132 °C). IR (KBr): 2922, 2852, 1589, 1539, 1352, 1153, 887, 835 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 7.34 (d, *J* = 8.0 Hz, 2 H), 7.53–7.59 (m, 5 H), 7.66 (dd, ^1J = 8.9 Hz, ^2J = 1.9 Hz, 1 H), 7.83 (s, 1 H), 7.85 (d, *J* = 1.9 Hz, 1 H), 8.09 (d, *J* = 8.0 Hz, 2 H), 8.16 (d, *J* = 8.9 Hz, 1 H). MS: *m*/*z* = 331.04 (34.88) [M + 2]$^+$, 329.05 (100.00) [M]$^+$, 294.10 (22.84), 201.12 (10.96), 176.12 (12.89), 146.89 (32.10), 91.16 (2.91), 51.13 (4.40).

6-Chloro-4-(2-chlorophenyl)-2-*p*-tolylquinoline (3l)

Mp 125–126 °C. IR (KBr): 2922, 2852, 1581, 1350, 1153, 1053, 881, 813 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 7.34 (d, *J* = 7.9 Hz, 2 H), 7.38–7.40 (m, 1 H), 7.45–7.49 (m, 3 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 7.66 (dd, ^1J = 9.0 Hz, ^2J = 2.2 Hz, 1 H), 7.81 (s, 1 H), 8.10 (d, *J* = 8.0 Hz, 2 H), 8.17 (d, *J* = 8.9 Hz, 1 H). ^{13}C NMR (125 M Hz, $CDCl_3$): δ = 22.69, 120.41, 124.34, 126.41, 127.44, 129.63, 129.72, 130.01, 130.07, 130.50, 131.35, 131.67, 135.47, 136.28, 139.81, 142.47, 147.05, 157.02, 160.73. MS: *m*/*z* = 366.96 (12.71) [M + 4]$^+$, 364.96 (65.56) [M + 2]$^+$, 362.97 (100.00) [M]$^+$, 361.96 (53.06), 327.99 (37.78), 293.05 (3.00), 146.34 (65.83), 145.49 (95.56), 144.50 (33.06), 132.44 (17.78), 91.10 (3.59), 51.06 (4.24). Anal. Calcd for $C_{22}H_{15}Cl_2N$ (363.06): C, 72.54; H, 4.15; N, 3.85. Found: C, 72.43; H, 4.20; N, 3.79.

6-Chloro-4-(2-fluorophenyl)-2-*p*-tolylquinoline (3m)

Mp 162 °C. IR (KBr): 3032, 2922, 2852, 1614, 1543, 1479, 1352, 1211, 1151, 887, 754 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 7.27–7.35 (m, 4 H), 7.44 (s, 1 H), 7.53 (s, 1 H), 7.63–7.67 (m, 2 H), 7.85 (s, 1 H), 8.09 (d, *J* = 6.9 Hz, 2 H), 8.16 (d, *J* = 10.3 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.69, 116.16, 116.34, 120.77, 124.33, 124.54, 126.54, 127.43, 129.64, 130.50, 130.76, 130.82, 131.67, 132.17, 136.28, 139.81, 142.47, 147.04, 157.02, 160.72. MS: *m*/*z* = 349.02 (35.04) [M + 2]$^+$, 347.04 (100.00) [M]$^+$, 346.03 (78.57), 312.07 (21.21), 155.85 (21.88), 145.49 (19.42), 91.12 (6.92). Anal. Calcd for $C_{22}H_{15}ClFN$ (347.09): C, 75.97; H, 4.35; N, 4.03. Found: C, 75.85; H, 4.41; N, 3.95.

6-Nitro-4-phenyl-2-*p*-tolylquinoline (3n)

Mp 202–203 °C. IR (KBr): 2922, 2850, 1593, 1548, 1483, 1336, 1180, 819, 746 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.46 (s, 3 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 7.56–7.64 (m, 5 H), 7.97 (s, 1 H), 8.16 (d, *J* = 8.0 Hz, 2 H), 8.32 (d, *J* = 9.2 Hz, 1 H), 8.48 (dd, ^1J = 9.2 Hz, ^2J = 2.5 Hz, 1 H), 8.85 (d, *J* = 2.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.70,

120.53, 122.91, 123.03, 124.74, 127.77, 129.13, 129.29, 129.48, 129.82, 131.67, 135.72, 137.02, 140.87, 145.30, 151.14, 159.99. MS: *m*/*z* = 340.07 (100.00) $[M]^+$, 310.09 (7.43), 294.10 (25.54), 293.10 (60.75), 202.05 (24.60), 176.02 (45.16), 145.72 (38.17), 139.18 (19.35), 91.04 (11.96), 77.03 (8.60), 57.01 (50.54). Anal. Calcd for $C_{22}H_{16}N_2O_2$ (340.12): C, 77.63; H, 4.74; N, 3.23. Found: C, 77.50; H, 4.80; N, 8.14.

6-Chloro-2-(4-methoxyphenyl)-4-phenylquinoline (3o)

Mp 135–136 °C (Lit.[10j] 135 °C). IR (KBr): 2916, 2850, 1587, 1516, 1026, 825, 777, 704 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.89 (s, 3 H), 7.04 (d, *J* = 8.7 Hz, 2 H), 7.54–7.57 (m, 5 H), 7.65 (dd, ^1J = 9.1 Hz, ^2J = 2.1 Hz, 1 H), 7.79 (s, 1 H), 7.84 (d, *J* = 2.2 Hz, 1 H), 8.14–8.18 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.42, 114.32, 119.55, 124.48, 126.26, 128.67, 128.81, 128.92, 129.46, 130.36, 131.50, 131.72, 131.80, 137.89, 147.22, 148.32, 156.60, 161.10. MS: *m*/*z* = 347.02 (35.27) $[M + 2]^+$, 345.03 (100.00) $[M]^+$, 344.02 (52.05), 310.06 (9.08), 301.06 (7.79), 155.21 (21.32), 132.71 (33.22), 120.50 (8.82), 99.17 (2.70).

6-Chloro-4-(2-chlorophenyl)-2-(4-methoxyphenyl) quinoline (3p)

Mp 140–141 °C. IR (KBr): 2958, 2852, 1602, 1541, 1469, 1373, 1247, 1157, 1022, 889, 771 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.89 (s, 3 H), 7.05 (d, *J* = 8.8 Hz, 2 H), 7.39 (dd, ^1J = 7.3 Hz, ^2J = 2.2 Hz, 1 H), 7.44–7.50 (m, 3 H), 7.61 (dd, ^1J = 7.5 Hz, ^2J = 1.4 Hz, 1 H), 7.65 (dd, ^1J = 9.6 Hz, ^2J = 2.2 Hz, 1 H), 7.78 (s, 1 H), 8.13–8.17 (m, 3 H).^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.42, 120.10, 124.36, 126.27, 126.99, 128.94, 130.08, 130.50, 131.36, 131.52, 131.66, 131.92, 133.35, 136.49, 145.59, 146.99, 156.58, 161.14. MS: *m*/*z* = 381.93 (17.57) $[M + 2]^+$, 379.92 (39.53) $[M]^+$, 378.93 (100.00), 343.96 (10.35), 265.02 (12.67), 176.09 (8.70), 154.29 (9.97), 132.51 (10.43), 99.14 (7.77), 57.12 (43.92), 55.13 (47.97). Anal. Calcd for $C_{22}H_{15}Cl_2NO$ (379.05): C, 69.49; H, 3.98; N, 3.68. Found: C, 69.31; H, 4.05; N, 3.60.

6-Chloro-4-(2-fluorophenyl)-2-(4-methoxyphenyl) quinoline (3q)

Mp 121 °C. IR (KBr): 2924, 2852, 1608, 1463, 1355, 1253, 1174, 1022, 825, 761 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.90 (s, 3 H), 7.05 (d, *J* = 8.7, 2 H), 7.28–7.32 (m, 1 H), 7.35 (t, *J* = 7.3, 1 H), 7.44 (dt, ^1J = 7.3 Hz, ^2J = 1.7 Hz, 1 H), 7.51–7.56 (m, 1 H), 7.61 (d, *J* = 1.9 Hz, 1 H), 7.65 (dd, ^1J = 8.9 Hz, ^2J = 2.2 Hz, 1 H), 7.82 (s, 1 H), 8.15 (t, *J* = 9.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.42, 114.32, 116.17, 116.34, 120.47, 124.33, 124.51, 124.54, 126.36, 126.54, 128.93, 130.49, 130.75, 130.82, 131.53, 131.62, 131.65, 131.97, 142.35, 156.61, 160.67, 161.13. MS: *m*/*z* = 365.01 (25.00) $[M + 2]^+$, 363.04 (96.00) $[M]^+$, 362.02 (30.25), 319.00 (35.50), 285.09 (50.50), 149.12 (67.00), 141.42 (55.75), 99.00 (26.50), 95.20 (65.00), 85.21 (70.00), 83.19 (95.00), 81.19 (87.00), 77.15 (27.00), 57.21 (95.00), 55.17 (100.00). Anal. Calcd for $C_{22}H_{15}ClFNO$ (363.08): C, 72.63; H, 4.16; N, 3.85. Found: C, 72.50; H, 4.21; N, 3.77.

2-(4-Methoxyphenyl)-6-nitro-4-phenylquinoline (3r)

Mp 221 °C. IR (KBr): 2922, 2852, 1643, 1593, 1479, 1253, 1095, 954, 796, 761 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.91 (s, 3 H), 7.07 (d, *J* = 8.8, 2 H), 7.56–7.64 (m, 5 H), 7.94 (s, 1 H), 8.24 (d, *J* = 8.8 Hz, 2 H), 8.29 (d, *J* = 9.3 Hz, 1 H), 8.47 (dd, 1 H, ^1J = 9.3 Hz, ^2J = 2.5 Hz, 1 H), 8.80 (d, *J* = 2.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.48, 114.48, 120.19, 122.92, 123.04, 124.54, 129.12, 129.26, 129.37, 129.45, 131.01, 131.48, 137.07, 145.15, 151.02, 151.20, 159.53, 161.81. MS: *m*/*z* = MS: 356.06 (100.00) $[M]^+$, 326.06 (2.85), 309.09 (25.00), 267.11 (6.84), 241.11 (5.38), 202.09 (8.29), 176.08 (12.95), 169.68 (8.10), 132.79 (16.58), 120.54 (9.20), 63.03 (8.00), 57.11 (4.81). Anal. Calcd for $C_{22}H_{16}N_2O_3$ (356.12): C, 74.15; H, 4.53; N, 7.86. Found: C, 74.29; H, 4.48; N, 7.78.

4-Methyl-2-phenylquinoline (3s)

Mp 63–65 °C (Lit.[10k] 65–67 °C). IR (KBr): 2924, 2854, 1648, 1553, 1458, 1242, 1161, 950, 748 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.72 (s, 3 H), 7.37–7.40 (m, 1 H), 7.44–7.51 (m, 3 H), 7.65–7.72 (m, 2 H), 7.95 (d, *J* = 8.3 Hz, 1 H), 8.08–8.14 (m, 3 H). MS: *m*/*z* = 219.00(100) $[M]^+$, 203.98 (12.68), 134.90 (48.59), 119.87 (67.61), 91.86 (80.28), 88.85 (78.87), 76.82 (85.21), 64.83 (83.80).

4-Methyl-2-*p*-tolylquinoline (3t)

Mp 53–54 °C (Lit.[10l] 51–53 °C). IR (KBr): 2925, 2854, 1658, 1615, 1462, 1245, 1162, 1112, 874, 754 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 2.70 (s, 3 H), 7.30–733 (m, 2 H), 7.48–7.52 (m, 1 H), 7.69–7.74 (m, 2 H), 7.97 (d, *J* = 8.3 Hz, 1 H), 8.07–8.10 (m, 2 H), 8.15–8.18 (m, 1 H). MS: *m*/*z* = 233.00 (62.28) $[M]^+$, 218.98 (60.53), 217.97 (35.53), 134.88 (30.26), 119.82 (53.95), 90.84 (75.00), 88.81 (84.65), 76.80 (67.54), 64.81 (100.00).