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FULL PAPER

Microwave-Assisted Metal-Free Rapid Synthesis of C4-Arylated Quinolines *via* Povarov Type Multicomponent Reaction

Devesh Chandra,[a] Ankit Kumar Dhiman,[a] Rakesh Kumar,[a] and Upendra Sharma*[a]

Abstract: Herein rapid microwave assisted, (±) camphor-10-sulfonic acid (CSA) promoted Povarov type multicomponent synthesis of 4-arylated quinolines from anilines, alkynes, and paraformaldehyde is described. This reaction proceeds through [4+2] cycloaddition of imine (formed *in situ* from aniline and paraformaldehyde) and alkynes in presence of CSA, without any metal catalyst. Mechanistic study revealed that CSA inhibit the synthesis of Troger's base and assist the cycloaddition of imine with alkyne by activating imine.

Keywords: Quinoline, alkyne, (±) camphor-10-sulfonic acid, Povarov reaction, microwave synthesis.

Introduction

For the synthesis and functionalization of quinolines, rapid transition metal-free/additive-free synthetic protocols are in high demand as quinoline scaffolds have been recognized as vital heterocyclic motifs obeying to their importance in natural products, pharmaceuticals, and material science.[1] Among them, 4-arylated quinolines possess excellent biological activities[2], and leading examples include yaequinolone[3] and peniprequinolone[4] (Figure 1). Substituted quinolines are also being used in dye stuff[5] and photonics.[6]

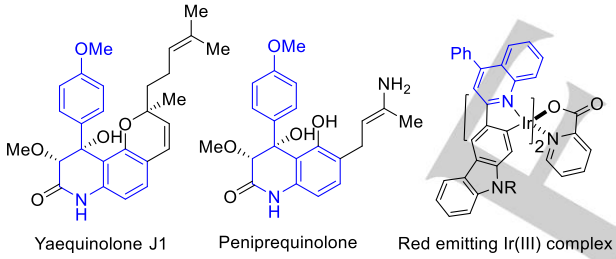
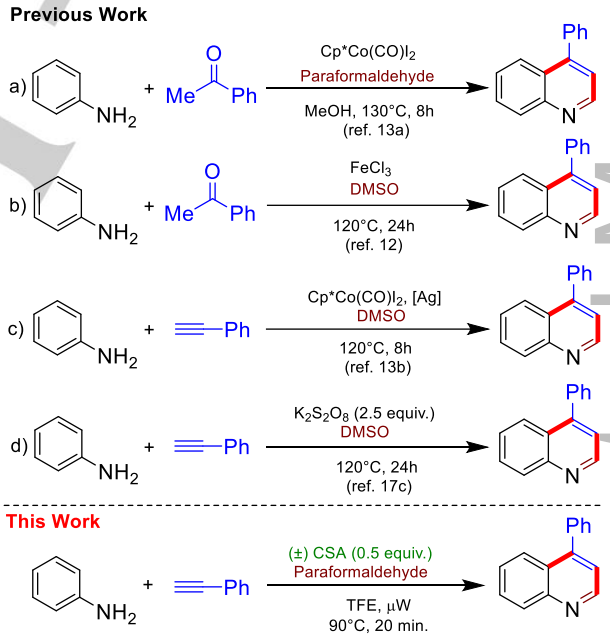


Figure 1. Representative examples of 4-aryl quinolines.

Obeying to the importance of 4-aryl quinolines, various methods have been developed for their synthesis. These includes Ni-catalyzed cyclization of 2-iodoanilines with alkynyl aryl ketones,[7] and Cu-catalyzed multicomponent synthesis of 2,4-disubstituted quinolines.[8] $FeCl_3$-catalyzed A_3-coupling of aniline, alkyne and aldehyde to provide 2,4-disubstituted quinolines,[9] and metal clay based catalysts has also been reported.[10] All these methods are only applicable for 2,4-disubstituted quinolines synthesis. Recently, Jiang and coworkers disclosed a Zn-promoted synthesis of 4-substituted quinoline from vinyl azides and anilines through dual synthon approach.[11]



Scheme 1. Seelected examples of 4-arylated quinoline synthesis.

Subsequently, Fe-catalyzed synthesis of 4-arylquinolines from aryl methyl ketones and aryl amine was reported by Jadhav and Singh (scheme 1b).[12] Co(III)-catalyst based C-H activation approches have also been utilized for the synthesis of 4-arylated quinolines.[13] First approch includes annulation of aryl methyl ketones and aryl amines using paraformaldehyde as the CO surrogate at 130 °C (Scheme 1a).[13a] Later, Yi et al. utlizes alkyne as coupling partner with aniline and DMSO as CO surrogate for the synthesis of 4-substuted quinolines at 120°C (Scheme 1c).[13b] Co(III)-catalyzed annulation of anilides with internal alkynes to form 3,4-diarylated quinolines has also been disclosed by Zhang[14] and Li[15] group independently. The removal of trace metal

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impurities from the final product particularly in pharmaceuticals can increase the overall process cost.[16]. Metal-free approaches are also described for the synthesis of aryl-substituted quinolines.[17] In this regard, recently Tiwari et. al.,[17c] developed a $K_2S_2O_8$ promoted metal-free protocol for the synthesis of quinoline *via* annulation of aniline and alkynes. (Scheme 1d). However use of excess $K_2S_2O_8$ limits the scope of this approach. In addition, long reaction time and high reaction temperature in all these reactions warrant further intervention.

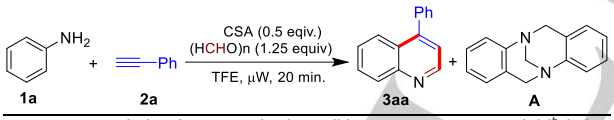
Traditionally, Povarov reaction[18] *i.e.* [4+2] cycloaddition of imines and olefins is a most anticipated method for the synthesis of substituted *N*-heterocycle. However, terminal alkynes and paraformaldehyde are rarely used in Povarov type reactions for 4-substituted quinolines synthesis.[19] On the other hand, mainly inorganic lewis acids[20] are known to promote this type of reaction, but the organic acid are rarely explored.[21] Intrestingly, acceleration of chemical reactions by organic molecules constitute a vibrant area in organic chemistry due to their ease of handling, stability, and environmental friendliness.[22]

Hence, in continuation of our group's research interest in the development of the methodologies for synthesis and functionalization[23] of quinolines, herein we describe a Povarov type multicomponent reaction for the synthesis of 4-substituted quinoline using (±) camphor-10-sulfonic acid (CSA) as the promotor.

Result and discussion

Initially, phenyl acetylene (0.1 mmol), aniline (0.12 mmol) and paraformaldehyde (0.125 mmol) were selected as model substrates and reacted under microwave irradiation at 90°C. Instead of desired 4-phenyl quinoline (**3aa**), troger's base[24] (**A**) was formed in good amount.

Table 1. Optimization study.[a]



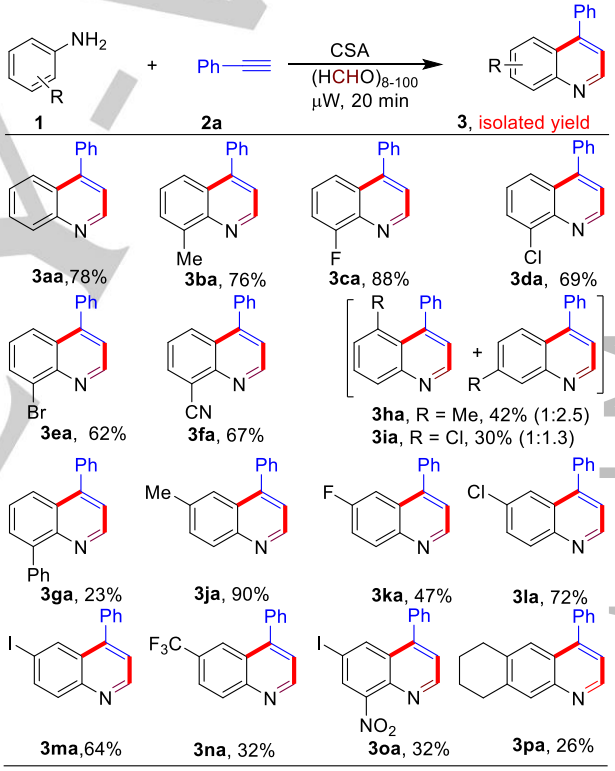
Entry	Deviation from standard conditions	Yield[b] (%)
1	no deviation	89
2	without CSA	nd[c]
3	without (HCHO)n	nd
4	MeOH instead of TFE	45
5	CoCp*(CO)I_2 instead of CSA	24
6	heating (24h) instead of μW	46
7	pivalic acid instead of CSA	40
8	triflic acid instead of CSA	68
9	admantane carboxylic acid instead of CSA	32
10	PTSA instead of CSA	<5

[a]Reaction conditions: anilines (**1a**; 0.12 mmol), alkynes (**2a**; 0.1 mmol), paraformaldehyde (0.125 mmol), CSA (0.05 mmol), TFE (0.2M), μW irradiation, 90 °C, 20 min.[b]GC yields by using *n*-decane as internal standard. [c]Troger's base A was formed

We screened different organic acids, i.e., pivalic acid, adamantane carboxylic acid, p-toluene sulfonic acid, triflic acid, and (±) camphor-10-sulfonic acid (CSA) for carrying out this transformation. This screening revealed CSA as the organic molecule of choice for promoting the formation of desired product **3aa**. Further screening of solvents provided TFE as an ideal solvent for the formation of **3aa** (89% yield. Table 1).

Under best optimal reaction conditions various substituted anilines (**1a-1p**) were allowed to couple with phenyl acetylene (**2a**, Table 2). Anilines substituted at o*rtho*-position with halogen, electron withdrawing and electron donating groups (**1a-1g**) provided C8-substituted quinolines in low to excellent yields (**3aa-3ga**, 23-88%). The *meta*-substituted anilines (**1h**, **1i**) also reacted with **2a** providing a regio-isomeric mixture of products (**3ha, 3ia**).

Table 2. Substrate scope with anilines.[a]



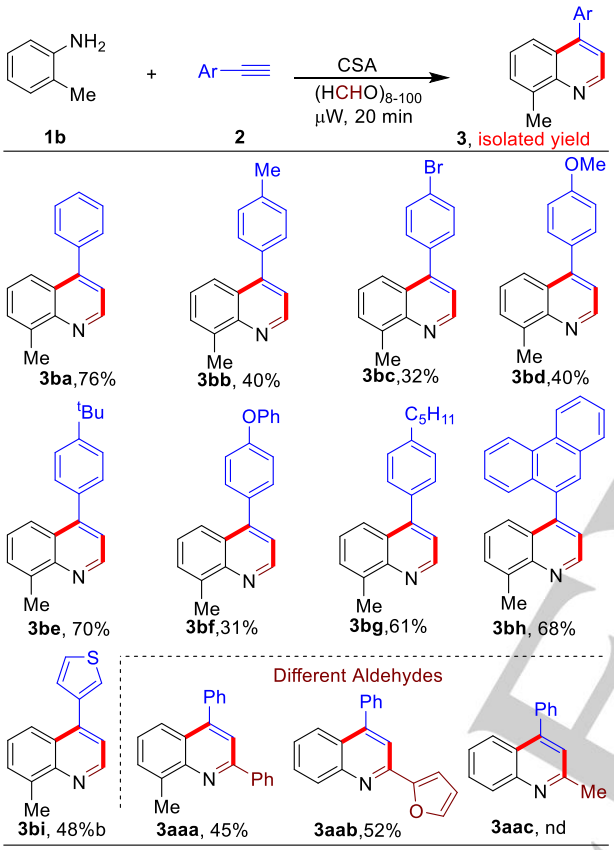
[a]Reaction conditions: anilines (**1a-p**; 0.36 mmol), alkynes (**2a**; 0.3 mmol), paraformaldehyde (0.375 mmol), CSA (0.15 mmol), TFE (0.2 M), μW irradiation, 90 °C, 20 min.; [b]30 min.

Similarly, the *para*-substituted anilines (**1j-1n**) were also compatible affording the desired products in low to good yields (**3ja-3na**, 32-90%). Disubstituted anilines such as 4-iodo-2-nitroaniline (**1o**) and 2-amino-5,6,7,8-tetrahydronaphthalene also reacted successfully albeit providing the corresponding desired product in low yields (**3oa** and **3pa**).

Next, various alkynes were reacted with *ortho*-toluidine (**1b**) (Table 3). Different *para*-substituted phenyl acetylenes (**2a-2g**) were well tolerated under optimal reaction conditions and provided the desired products in 31-76% yields (**3ba-bg**). The

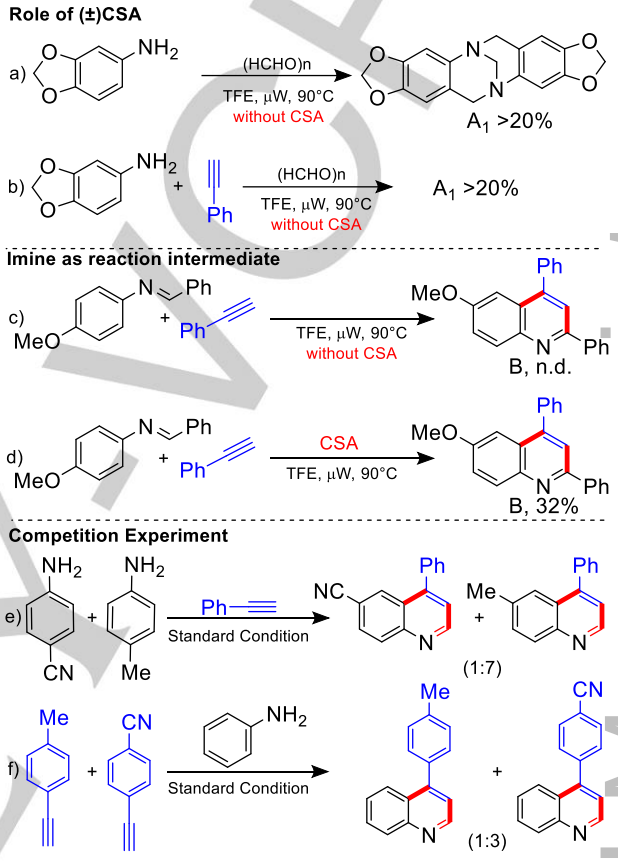
polyaromatic alkyne (**2h**) also gave the desired product (**3bh**) in good yield. Although 3-ethynylthiophene provided the desired product **3bi** in 48% of yield, 2-ethynylpyridine failed to react. Internal alkyne did not react under current reaction conditions. Further, we examined different aldehydes (**4a-4c**) as a substitute of paraformaldehyde. Benzaldehyde and furfural were found suitable substrates but acetaldehyde failed to react.

Table 3. Substrate scope with alkynes.[a]



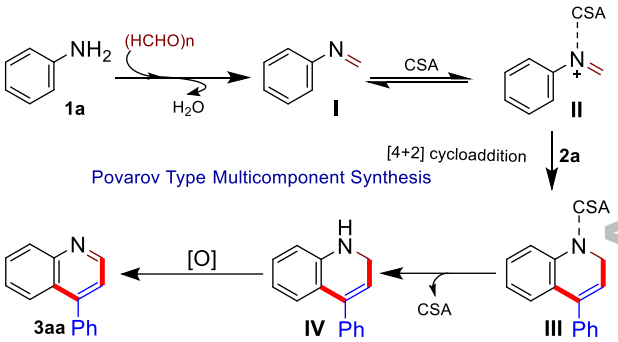
[a]Reaction conditions: anilines (**1a**-**b**; 0.36 mmol), alkynes (**2a**-**k**; 0.3 mmol), paraformaldehyde (0.375 mmol), CSA (0.15 mmol), TFE (0.2 M), μW irradiation, 90 °C, 20 min. [b]30 min.

For the preliminary understanding of the reaction pathway, few experiments were carried out. The standard reaction as well as the reaction between aniline and paraformaldehyde without CSA afforded troger's base as the only product (Scheme 2a and 2b). These reactions confirm the role of CSA in promoting the reaction *via* inhibiting the formation of the troger's base. The reaction of *N*-(4-methoxyphenyl)-1-phenylmethanimine (**II**) with **2a**, in the presence of CSA, afford the product **B** in 32% yield whereas no product was observed without CSA (Scheme 2c and 2d). These two experiments confirm imine (**II**) as possible intermediate and the role of CSA in promoting cycloaddition between imine and alkynes *via* activating imine. Furthermore, a competition experiment between **1j** (*p*-Me) and **1q** (*p*-CN) with **2a** provides the corresponding products in 7:1 ratio (Scheme 2e); on the other hand, competition experiment between **2b** (*p*-Me) and **2l** (*p*-CN) with **1a** provides corresponding products in 1:3 ratio (Scheme 2f).[24] These experiments disclosed that imine with electron donating group and alkyne with electron withdrawing group favors the annulations for the synthesis of 4-arylated quinolines.



Scheme 2. Control Experiments.

On the basis of thses experiments and literature,[17a, 20c] a plausible reaction mechanism for the synthesis of 4-arylated quinoline is proposed (Scheme 3).



Scheme 3. Plausible mechanism for quinolines synthesis.

The reaction may proceed through the formation of *in situ* generated intermediate **I** from the condensation of aniline and paraformaldehyde. Cycloaddition of **2a** with CSA activated

imine (**II**) *via* a Povarov type multicomponent reaction afforded intermediate **IV**, which on spontaneous oxidation yield the final product **3aa**.

Conclusions

In summary, we have developed a rapid microwave-assisted metal-free method for the synthesis of 4-substituted quinolines by using an organic molecule as an acid promotor.

Experimental Section

General Methods

Reagent Information: All experiments were performed in CEM Discover using SynergyTM software. High-resolution mass spectra were recorded by Q-TOF using the electrospray ionization (ESI-TOF) method. All chemicals were purchased from the Sigma-Aldrich and TCI. TLC plates (Aluminium sheet silica gel 60 F254) were purchased from Merck. Flash chromatography was performed over silica gel (230−400 mesh) using n-hexane and ethyl acetate as eluents.

Analytical Information: The melting points were recorded on a Bronsted Electro thermal 9100. All isolated compounds are characterized by ^{1}H NMR, ^{13}C NMR, LC–MS, and IR. In addition, all of the compounds are further characterized by HRMS. Mass spectra were recorded on Water Q-ToF Micro mass spectrometer. IR was analyzed by Shimadzu IR Prestige-21with ZnSe Single reflection ATR accessory. Nuclear magnetic resonance spectra were recorded on a Bruker-Avance 600 or 300 MHz instrument. All ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26). All ^{13}C NMR spectra were reported in ppm relative to deuterated chloroform (77.23) and all were obtained with ^{1}H decoupling. Optimization studies were done by GC by using *n*-decane as an internal standard.

General Procedure for Synthesis of 4-substituted quinolines: To a solution of phenylacetylene (0.3 mmol) in TFE (0.2M), paraformaldehyde (0.375 mmol) aniline (0.36 mmol) and (±) camphor-10-sulfonic acid (0.15 mmol) were added in a glass reaction tube with sealed cap and irradiate with microwave in CEM Discover using Synergy™ software for 20 min. or until the full conversion monitored by standard monitoring tools *i.e* TLC at 100 °C. The crude reaction mixture was concentrated at reduced pressure. Isolation and purification were done by flash chromatography using *n*-hexane and ethyl acetate mixture as an eluent.

Characterization data

4-phenylquinoline (Table 1, entry **3aa**). Yellow liquid (78 mg, 78%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.95 (d, *J* = 4.2 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.71-7.76 (m, 1H), 7.48-7.53 (m, 6H), 7.34 (d, *J* = 4.2 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1, 148.8, 148.7, 138.1, 129.9, 129.7(2C), 129.5, 128.7(2C), 128.6, 126.9, 126.8, 126.0, 121.5 ppm. IR (ZnSe): ν_{max} = 3055, 2925, 1573, 1490, 1390, 1276, 1029, 850, 767, 655 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{15}H_{12}N$ 206.0964, found 206.0951.

8-methyl-4-phenylquinoline (Table 1, entry **3ba**). Pale yellow liquid (50 mg, 76%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.98 (d, *J* = 4.2 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 6.3 Hz, 1H), 7.48-7.53 (m, 5H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.33–7.36 (m, 1H), 2.88 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.86, 148.84, 147.9, 138.7, 137.5, 129.73 , 129.67, 128.6 , 128.4, 126.9, 126.4, 124.1, 121.3, 18.8 ppm; IR (ZnSe): ν_{max} = 3033, 2920, 1587, 1489, 1402, 1350, 1091, 852, 767, 702 cm^{-1}; HRMS (ESI-TOF): m/z $[M+H]^+$ calcd for $C_{16}H_{14}N$ 220.1121, found 220.1111.

8-fluoro-4-phenylquinoline (Table 1, entry **3ca**). White crystal (59 mg, 88%). m.p. 81.8-82°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.00 (d, *J* = 3.6 Hz, 1H), 7.76-7.66 (m, 1H), 7.57-7.51 (m, 3H), 7.52-7.49 (m, 2H), 7.46-7.40 (m, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3) δ = 150.1, 148.5, 137.8, 129.6, 128.8, 128.8, 122.5, 121.8, 113.5, 113.4 ppm; ^{19}F NMR (565 MHz, $CDCl_3$): δ = 124.8. IR (ZnSe): ν_{max} = 3033, 2916, 1562, 1489, 1402, 1392, 1068, 877, 694 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd for $C_{15}H_{11}N$ 224.0870, found 224.0860.

8-chloro-4-phenylquinoline (Table 1, entry **3da**). Yellow liquid (49 mg, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.07 (d, J = 4.2 Hz, 1H), 7.84-7.87 (m, 2H), 7.51-7.55 (m, 3H), 7.47-7.49 (m, 2H), 7.40-7.43 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ= 150.6, 149.3, 145.1, 137.8, 134.0, 129.67, 129.66 (2C), 128.82, 128.80(2C) 128.4, 126.5, 125.3, 122.4; IR (ZnSe): ν_{max} (cm-1) 3036, 2922, 1585, 1489, 1444, 1386, 1033, 856, 761; HRMS (ESI-TOF): m/z $[M+H]^+$ calcd for $C_{15}H_{11}ClN$, 240.0475 found 240.0560.

8-bromo-4-phenylquinoline (Table 1, entry **3ea**). Yellow liquid (52 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.07 (d, *J* = 4.8 Hz, 1H), 8.07 (dd, *J* = 7.2 Hz, *J* = 1.2 Hz 1H), 7.88 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz 1H), 7.50-7.54 (m, 3H), 7.46-7.48 (m, 2H), 7.40 (d, *J* = 4.2 Hz, 1H), 7.34 (t, *J* = 7.8 Hz 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 150.8, 149.4, 145.8, 137.7, 133.3, 129.7, 128.79, 128.77 , 128.4, 127.0, 126.1, 125.4, 122.3 ppm; IR (ZnSe): ν_{max} () 3036, 2922, 1585, 1489, 1444, 1386, 1033, 856, 761 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{15}H_{11}BrN$ 284.0069, found 284.0052.

4-phenylquinoline-8-carbonitrile (Table 1, entry **3fa**). White crystal (46 mg, 67%); m.p. 138-139.8 °C. ^{1}H (600 MHz, $CDCl_3$) δ = 9.16 (d, *J* = 4.2 Hz, 1H), 8.21-8.17 (m, 2H), 7.65- 7.55 (m, 4H), 7.55-7.48 (m, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 152.1, 149.3, 148.2, 135.6, 131.3, 129.6, 129.1, 129.0, 127.0, 125.9, 123.0, 117.6ppm. IR (ZnSe): ν_{max} () 2922, 2225, 1745, 1556, 1282, 1033, 798, 653 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{16}H_{11}N_2$ 231.0917, found 231.0923.

4,8-diphenylquinoline (Table 1, entry **3ga**). White solid (19 mg, 23%); m.p. 252-253 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.97 (d, *J* = 4.8 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.71-7.74 (m, 3H), 7.50-7.56 (m,8H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.35 (d, *J* = 4.2 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ =149.8, 148.7, 146.6, 141.4, 140.1, 138.6, 130.8 (2C), 130.4, 129.8, 128.7, 128.5, 128.1, 127.5, 127.4, 126.3, 125.8, 121.4 ppm. IR (ZnSe): ν_{max} = 3031, 1563, 1480, 1394, 1287, 1156, 1070, 840, 765, 700 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{21}H_{16}N$ 282.1277, found 282.1280.

Regioisomeric mixture of 7-methyl-4-phenylquinoline and 5-methyl-4-phenylquinoline (Table 1, entry **3ha**). Yellow liquid (28 mg, 42%, a:b :: 1:2.5). ^{1}H NMR (600 MHz, $CDCl_3$) (isomer a) δ = 8.90 (d, *J* = 4.2 Hz, 1H), 7.95 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.48-7.54 (m, 5H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 4.2 Hz, 2H), 2.58 (s, 3H) ppm ;^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.7, 148.8, 148.6, 142.4, 135.7, 129.9, 128.9, 128.8, 127.9, 127.8, 126.3, 123.5, 24.5 ppm; ^{1}H NMR (600 MHz, $CDCl_3$) (isomer b): δ = 8.86 (d, *J* = 4.2 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.46-7.42 (m, 3H), 7.34-7.32 (m, 3H), 2.02 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) (isomer b): δ = 149.9, 149.0, 139.6, 138.1, 129.5, , 128.9, 128.6, 128.5, 128.3, 127.9, 125.5, 124.7, 120.6, 19.6

ppm. IR (ZnSe): v_{max} = 2928, 1632, 1575, 1459, 1244, 1196, 827, 759, 700 cm^{-1}. HRMS (ESI-TOF): m/z M+H]$^+$ calcd. for $C_{16}H_{14}N$ 220.1121, found 220.1112.

Regioisomeric mixture of 7-methyl-4-phenylquinoline and 5-methyl-4-phenylquinoline (Table 1, entry **3ia**). Pale yellow liquid (21 mg, 30%) (a: b :: 1: 1.3). ^{1}H NMR (600 MHz , $CDCl_3$): (isomer a): δ = 8.94 (d, *J* = 4.2 Hz, 1H), 8.17 (d, *J* = 1.8 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.49-7.47 (m, 2H), 7.42-7.43 (m, 4H) 7.31 (d, *J* = 4.2 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 151.0, 149.1, 148.6, 140.8, 137.5, 135.3, 129.5, 128.93, 128.73, 127.6, 127.3, 125.2, 121.5 ppm; ^{1}H NMR (600 MHz, $CDCl_3$) (isomer b): δ = 8.91 (d, *J* = 4.8 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.25-7.64 (m, 1H), 7.58 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.50-7.56 (m, 3H), 7.33-7.35 (m, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.1, 149.6, 148.3, 140.8, 130.8, 129.7, 128.9, 129.65, 128.72, 127.7, 124.9, 124.6, 121.5 ppm. IR (ZnSe): v_{max} = 3036, 2922, 1585, 1489, 1444, 1386, 1033, 856, 761 cm^{-1}. HRMS (ESI-TOF) m/z [M+H]$^+$ calcd. for $C_{15}H_{11}ClN$ 240.0575, found 240.0560.

6-methyl-4-phenylquinoline (Table 1, entry **3ja**). Orange liquid (59 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.87 (d, *J* = 4.5 Hz, 1H), 8.07 (d, *J* = 8.7 Hz, 1H), 7.66 (s, 1H), 7.48-7.54 (m, 6H), 7.28 (d, *J* = 4.5 Hz, 1H), 2.46 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.2, 148.1, 147.1, 137.5, 132.8, 131.6, 130.5, 129.6, 128.96, 128.91, 127.7, 124.8, 122.2, 21.9; IR (ZnSe): v_{max} () 2922, 1622, 1574, 1462, 1244, 1190, 827, 759, 700 cm^{-1}. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd. for $C_{16}H_{14}N$ 220.1121, found 220.1109.

6-fluoro-4-phenylquinoline (Table 1, entry **3ka**). Yellow liquid (31 mg, 47%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.91 (d, *J* = 4.8 Hz, 1H), 8.16-8.19 (m, 1H), 7.47-7.55 (m, 7H), 7.36 (d, 3.6Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.6, 159.9, 149.4, 148.2, 145.9, 137.7, 132.5, 132.4, 129.5, 128.9, 128.8, 127.8, 127.7, 121.9, 119.8, 119.6ppm. IR (ZnSe): v_{max} = 2924, 1622, 1564, 1492, 1242, 914, 700, 613 cm^{-1}. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd. for $C_{15}H_{11}FN$ 224.0870, found 224.0883.

6-chloro-4-phenylquinoline (Table 1, entry **3la**). Yellow solid (52 mg, 72%); m.p. 66.2- 66.8°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.94 (d, *J* = 4.8 Hz, 1H), 8.12 (d, *J* = 9.0 Hz, 1H), 7.89 (d, *J* = 1.8 Hz, 1H), 7.67 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.52-7.57 (m, 3H), 7.48-7.49 (m, 3H), 7.37 (d, *J* = 4.8 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 150.2, 148.1, 147.1, 137.5, 132.8, 131.6, 130.5, 129.6,128.96, 128.91, 127.7, 124.8, 122.2. IR (ZnSe): v_{max} = 2920, 16.6, 1583, 1489, 1352, 1155, 1076, 970, 773, 698 cm^{-1}. HRMS (ESI-TOF): [M+H]$^+$ m/z calcd. for $C_{15}H_{11}ClN$ 240.0575, found 240.0570.

6-iodo-4-phenylquinoline (Table 1, entry **3ma**). Yellow solid (63 mg, 64%); m.p. 99.0-99.4°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.94 (d, *J* = 4.2 Hz, 1H), 8.28 (d, *J* = 1.8 Hz , 1H), 7.97 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.91 (d, *J* = 9.0 Hz, 1H), 7.53-7.57 (m, 3H), 7.48-7.49 (m, 2H), 7.35 (d, *J* = 4.2 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 150.4, 147.8, 147.6, 138.4, 137.4, 134.8, 131.5, 129.6, 128.98, 128.94, 128.7, 122.1, 92.9 ppm; IR (ZnSe) v_{max} () : 2926, 1479, 1348, 1149, 1033, 964, 819, 702, 617 cm^{-1}. HRMS (ESI-TOF) m/z [M+H]$^+$ calcd. for $C_{15}H_{11}IN$ 331.9931, found 331.9942.

4-phenyl-6-(trifluoromethyl) quinoline (Table 1, entry **3na**). Yellow liquid (29 mg, 32%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.13 (d, *J* = 4.2 Hz, 1H), 8.17-8.33 (d, *J* = 8.4 Hz, 1H), 8.27 (s, 1H), 7.93 (d, *J* = 10.7 Hz, 1H), 7.65-7.56 (m, 3H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 4.4 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 152.2, 149.7, 148.2, 136.9, 135.6, 131.3, 129.6, 129.2, 129.0, 127.0, 125.9, 123.0, 117.7, 113.7 ppm; 19F NMR (565 MHz, $CDCl_3$) δ = -62.25 ppm. IR (ZnSe): v_{max} = 2981, 2922, 2864, 1726, 1587, 1309, 1163, 1055, 1012, 812, 761, 702 cm-1. HRMS (ESI-TOF) m/z [M+H]$^+$ calcd for $C_{16}H_{11}CF_3N$ 240.0575, found 240.0570.

6-iodo-8-nitro-4-phenylquinoline (Table 1, entry **3oa**). Orange solid (36 mg, 32%); m.p. 102-104°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.07 (d, *J* = 4.2 Hz, 1H), 8.45 (s, 1H), 8.22 (s, 1H), 7.57-7.59 (m, 3H), 7.45-7.49 (m, 3H) ppm.^{13}C NMR (75 MHz, $CDCl_3$) δ = 152.4, 149.1, 147.9, 139.3, 138.7, 136.4, 131.7, 129.56 (2C), 129.52, 129.3(2C), 123.7, 88.8 ppm. HRMS (ESI-TOF) m/z [M+H]$^+$ calcd. for $C_{15}H_{10}IN_2O_2$ 376.9781, found 376.9790.

4-phenyl-6,7,8,9-tetrahydrobenzo[*g*]quinoline (Table 1, entry **3pa**). Reddish brown liquid (20 mg, 26%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.94 (d, *J* = 4.8 Hz, 1H), 7.64 (d, *J* = 8.4, 1H), 7.47-7.53 (m, 5H), 7.29 (d, *J* = 4.2 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 3.39-3.41 (m, 3H), 2.93-2.96 (m, 3H), 1.97-2.00 (m, 2H), 1.89-1.94 (m, 2H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 148.8, 148.5, 147.5, 138.7, 138.4, 134.9, 129.7, 129.1, 128.6, 128.4, 125.0, 122.9, 120.7, 30.5, 25.4, 23.2, 23.0ppm. IR (ZnSe): v_{max} = 2927, 2862, 1668, 1435, 1278, 1155, 1028, 968, 781, 700, 675 cm^{-1}. HRMS (ESI-TOF): m/z [M+H]$^+$ calcd. for $C_{19}H_{18}N$ 260.1434, found 260.1450.

8-methyl-4-(p-tolyl)quinoline (Table 2, entry **3bb**). Yellow liquid (28 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.96 (d, *J* = 4.2 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.37-7.40 (m, 3H), 7.32-7.34 (m, 3H), 2.87 (s, 3H), 2.47 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.8, 148.8, 147.9, 138.3, 137.5, 135.7, 129.7, 129.6, 129.3, 127.0, 126.3, 124.2, 121.3, 21.4, 18.8 ppm. IR (ZnSe): v_{max} = 3369, 2927, 1610, 1498, 1450, 1398, 1276, 1111, 1037, 819, 765, 723 cm^{-1}. HRMS (ESI-TOF) m/z [M+H]$^+$ calcd. for $C_{17}H_{16}N$ 234.1277, found 234.1289.

4-(4-bromophenyl)-8-methylquinoline (Table 2, entry **3bc**). Yellow liquid (29 mg, 32%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.97 (d, *J* = 4.3 Hz, 1H), 7.71-7.67 (m, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.59 (dt, *J* = 7.0, 1.3 Hz, 1H), 7.40 (dd, *J* = 8.4, 7.0 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 4.3 Hz, 1H), 2.87 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 148.8, 148.8, 147.9, 138.3, 137.4, 135.6, 129.6, 129.6, 129.3, 127.0, 126.2, 124.1, 121.3, 21.4, 18.8 ppm. IR (ZnSe): v_{max} () 2930, 1668, 1593, 1483, 1406, 1390, 1274, 1072, 1008, 825, 800, 765, 721 cm^{-1}. HRMS (ESI-TOF): calcd m/z [M+H]$^+$ for $C_{16}H_{13}BrN$ 298.0026, found 298.0218.

4-(4-methoxyphenyl)-8-methylquinoline (Table 2, entry **3bd**). Yellow liquid (29 mg, 40%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.96 (d, *J* = 4.2 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.41-7.37 (m, 1H), 7.05 (d, *J* = 9.0 Hz, 2H), 3.90 (s, 3H), 2.87 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 159.9, 148.7, 130.9, 130.8, 129.6, 129.3, 127.0, 126.2, 124.1, 121.2, 114.3, 114.1, 55.5, 18.8 ppm. IR (ZnSe): v_{max} = 2958, 1648, 1483, 1367, 1224, 1145,760, 720 cm^{-1}. HRMS (ESI-TOF): m/z [M+H]$^+$ calcd. for $C_{17}H_{16}NO$ 250.1226, found 250.1204.

4-(4-(tert-butyl) phenyl)-8-methylquinoline (Table2, entry **3be**). White solid (96 mg, 70%); m.p. 126.0- 127.0°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.97 (d, *J* = 4.2 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.54 (d, J = 7.8 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.38-7.40 (m, 1H), 7.34 (d, *J* = 4.8 Hz, 1H), 2.87 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 151.5, 148.89, 148.84, 147.9, 137.4, 135.6, 129.6, 129.5, 127.0, 126.2, 125.6, 124.3, 121.3, 34.9, 31.5, 18.9 ppm. IR (ZnSe): v_{max} = 2953, 2922, 1680, 1500, 1363, 1269, 1109, 833, 771

cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{20}H_{22}N$ 276.1747, found 276.1759.

8-methyl-4-(4-phenoxyphenyl) quinoline (Table2, entry **3bf**). Yellow liquid (48 mg, 31%). ^1H NMR (600 MHz, $CDCl_3$) δ = 8.97 (d, *J* = 4.2 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.39-7.42 (m, 3H), 7.33 (d, *J* = 4.2 Hz, 1H), 7.13-7.19 (m, 5H), 2.88 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 157.8, 156.7, 148.7, 148.1, 147.8, 137.4, 133.1, 131.1, 129.9, 129.6, 126.8, 126.3, 123.91, 123.86, 121.2, 119.5, 118.4, 18.7 ppm; IR (ZnSe): ν_{max} 2951, 2922, 1672, 1587, 1487, 1396, 1232, 1166, 767, 748, 692 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{22}H_{18}NO$ 312.1383, found 311.6693.

8-methyl-4-(4-pentylphenyl) quinoline (Table2, entry **3bg**). Colourless liquid (88 mg, 61%). ^1H NMR (600 MHz, $CDCl_3$) δ = 8.96 (d, *J* = 4.2 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.37-7.42 (m, 3H), 7.33 (dd, *J* = 6.6, 1.8 Hz, 3H), 2.88 (s, 3H), 2.71 (t, *J* = 7.8 Hz ,2H), 1.68-1.74 (m, 2H), 1.40 (dq, *J* = 7.2, 3.6 Hz, 4H), 0.94 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 148.9, 148.8, 147.9, 143.4, 137.4, 135.8, 129.64, 129.60, 128.6, 126.9, 126.2, 124.2, 121.3, 35.9, 31.7, 31.3, 22.7, 18.8, 14.2 ppm; IR (ZnSe): ν_{max} = 2922, 2868, 1680, 1496, 1398, 1118, 817, 765, 732 cm^{-1}; HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{21}H_{24}N$ 290.1903, found 290.1893.

8-methyl-4-(phenanthren-9-yl) quinoline (Table 2, entry **3bh**). Colourless liquid (46 mg, 48%); ^1H NMR (600 MHz, $CDCl_3$) δ = 9.10 (d, *J* = 4.2 Hz, 1H), 8.82 (d, *J* = 8.4 Hz, 1H), 8.79 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 2H), 7.65-7.68 (m, 2H), 7.58 (d, *J* = 7.2, 1H), 7.49 (d, *J* = 4.2 Hz, 1H), 7.41 -7.43 (m, 1H), 7.35-7.39 (m, 2H), 7.23-7.25 (m, 1H), 2.94 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 148.9, 147.71, 147.65, 137.5, 134.9, 131.4, 131.3, 130.6, 130.5, 129.9, 128.9, 128.32, 128.28, 127.3, 127.23, 127.16, 126.96, 126.94, 126.49, 124.7, 123.1, 122.8, 122.51, 18.7 ppm; IR (ZnSe): ν_{max} = 3419, 3296, 1592, 1402, 1249, 1211, 1006, 758 cm^{-1}; HRMS (ESI-TOF): m/z $[M+Na]^+$ calcd. for $C_{24}H_{18}N$ 341.1175, found 342.7653.

8-methyl-4-(thiophen-2-yl)quinoline (Table 2, entry **3bi**). Yellow solid (32 mg, 48 %; m.p. 76.0-77.0°C. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.95 (d, *J* = 4.2 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 6.6 Hz, 1H), 7.50 – 7.51 (m, 2H), 7.41-7.43 (m, 1H), 7.38 (d, *J* = 4.2 Hz, 1H), 7.33-7.34 (m, 1H), 2.86 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 149.1, 148.2, 143.8, 139.3, 137.8, 129.9, 129.4, 127.2, 126.7, 126.4, 125.2, 124.1, 121.4, 18.9 ppm; IR (ZnSe): ν_{max} = 3086, 2922, 1664, 1587, 1496, 1413, 1085, 1041, 850, 771, 698 cm^{-1}; HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{14}H_{12}SN$ 226.0685, found 226.0679.

8-methyl-2,4-diphenylquinoline (Table 3, entry **3aaa**). Brown resin (39 mg, 45%). ^1H NMR (600 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 7.2 Hz, 2H), 7.86 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.58-7.50 (m, 7H), 7.49-7.45 (m, 1H), 7.39-7.33 (m, 1H), 2.97 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 148.89, 148.85, 147.91, 138.31, 137.46, 135.69, 129.65, 129.61, 129.32, 127.00, 126.26, 124.19, 121.30, 21.43, 18.80 ppm. IR (ZnSe): ν_{max} = 2918, 1591, 1554, 1485,1355, 1178, 1095, 1028, 763, 690 cm^{-1}. HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{22}H_{18}N$ 296.1434, found 296.1456.

2-(furan-2-yl)-4-phenylquinoline (Table 3, entry **3aab**). Black resin (42 mg, 52%). ^1H NMR (600 MHz, $CDCl_3$) δ = 8.23 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.80 (s, 1H), 7.74 (t, *J* = 8.2 Hz, 1H), 7.65 (s, 1H), 7.58 (d, *J* = 4.3 Hz, 4H), 7.55 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 3.4 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 153.9, 149.3, 148.8, 148.7, 144.3, 138.3, 129.9, 129.9, 129.7, 128.7, 128.6, 126.4, 125.9, 125.9, 117.9, 112.4, 110.3 ppm. IR (ZnSe): ν_{max} = 1591, 1573, 1492, 1409, 1008, 883, 632, 698 cm^{-1}; HRMS (ESI-TOF): m/z $[M+H]^+$ calcd. for $C_{19}H_{14}NO$ 272.1070, found 272.1054.

6H,13H-5,12-methano[1,3]dioxolo[4',5':4,5]benzo[1,2 b][1,3]dioxolo[4',5':4,5]benzo[1,2-f][1,5]diazocine (Scheme 1, $\mathbf{A_1}$). ^1H NMR (600 MHz, $CDCl_3$) δ = 6.61 (s, 2H), 6.34 (s, 2H), 5.86 (d, *J* = 1.2 Hz, 2H), 5.83 (d, *J* = 1.2 Hz, 2H), 4.54 (d, *J* = 16.4 Hz, 2H), 4.22 (s, 2H), 3.97 (d, *J* = 16.4 Hz, 2H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 146.8, 144.6, 141.6, 120.0, 105.9, 105.6, 100.9, 67.1, 58.4 ppm.

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[24] See *Supporting Information*

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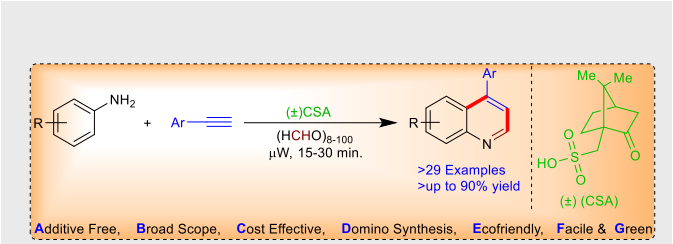
FULL PAPER

Quinoline Synthesis: Three component reaction of aniline, alkynes and formaldehyde under microwave irradiation promoted by CSA led to the formation of 4-arylated quinolines *via* Povarov type reaction.



Key Topic Quinoline Synthesis*

*Devesh Chandra, Ankit Kumar Dhiman, Rakesh Kumar, and Upendra Sharma**

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Microwave-Assisted Metal-Free Rapid Synthesis of C4-Arylated Quinolines *via* Povarov Type Multicomponent Reaction