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Copper(II) triflate catalyzed three-component reaction for the synthesis of 2,3-diarylquinoline derivatives using aryl amines, aryl aldehydes and styrene oxides†

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An efficient and expedient synthetic protocol is reported for the synthesis of 2,3-diarylquinoline derivatives from readily available aryl amines, aryl aldehydes and styrene oxides using 10 mol% copper(II) triflate by employing three-component reaction. This approach involves the reaction between the *in situ* generated imine (derived from the aryl amine and aryl aldehyde) and styrene oxide, which enables the formation of the desired products. The present method has several advantages such as high atom-economy, high regioselectivity, easy handling, consecutive one C–N and two C–C bond formation, shorter reaction time and broader substrate scope with good yields.

Introduction

Multicomponent reactions (MCRs) are well-known and well established synthetic approaches, which are extensively explored in the synthesis of bioactive heterocycles, and combinatorial and medicinal chemistry.[1a] These reactions are usually one-pot reactions, in which three or more reactants react sequentially to form a product, where all or most of the atoms incorporate into the structure of the newly formed product.[1b–f] The notable features of this class of reactions are atom economy, efficiency, diversity, speed and environmentally benign nature.[2a,b] Over the years, the synthetic community has made much effort in designing new MCRs for the construction of structurally complex molecules due to numerous advantages.[2–4] The quinoline backbone is present in many naturally occurring compounds, namely in the alkaloids. Numerous alkaloids containing the quinoline moiety have been marketed as potent drugs.[5a] In addition to that, related natural products are found to exhibit a wide range of biological activities, such as antimalarial,[5b] anticancer,[5c,d] antituberculosis,[5e,f] and anti-HIV activities.[5g] Moreover, naturally occurring cinchonidine and quinine are used as chiral ligands in asymmetric synthesis.[6a–d] Furthermore, quinoline and its derivatives have been extensively used in materials science.[7] Due to their wide applications in diverse fields, the synthetic community has made tremendous efforts to develop a new method for synthesizing quinoline and its derivatives. Some classical syntheses for obtaining quinolines are Skraup,[8a] Conrad–Limpach,[8b] Pfitzinger,[8c,d] Doebner–Von Miller,[8e] Friedlaender[8f] and many other methods.[9] To date, very few methods have been developed for the synthesis of 2,3-diarylquinoline derivatives. Recently, Verma *et al.* reported the synthesis of 2,3-diarylquinoline derivatives by KOH mediated cycloaddition reaction of *o*-aminobenzyl alcohols and internal alkynes (Scheme 1a).[10] Similarly, Wu *et al.* demonstrated the synthesis of 2,3-diarylquinolines from the reaction of substituted aryl amines with two different amino acids in the presence of I_2 and HI (Scheme 1b).[11] Likewise, Reddy *et al.* showed an approach for the synthesis of 2,3-diarylquinoline skeletons using 2-azido phenyl propargylic alcohols and aryl boronic acids in the presence of a $Ni(acac)_2$ catalyst (Scheme 1c).[12]

Despite the usefulness of the above-mentioned methods, they have some demerits, such as longer reaction time,[10] requirement of expensive starting materials,[12] and harsh reaction conditions.[10–12] Thus, it is desirable to devise easy and economically viable general synthetic methodology to access the 2,3-diarylquinoline scaffolds. Copper(II) triflate has emerged as a powerful catalyst in organic synthesis, due to its stability, low toxicity and easy handling.[13a,b] In recent years, it has been used as an efficient catalyst in promoting several organic transformations, such as cross-coupling,[13c] oxidative ring closure,[13d] and aziridination.[13e] Our research group has demonstrated the synthesis of a variety of quinoline derivatives using a multi-component reaction,[14a] and other

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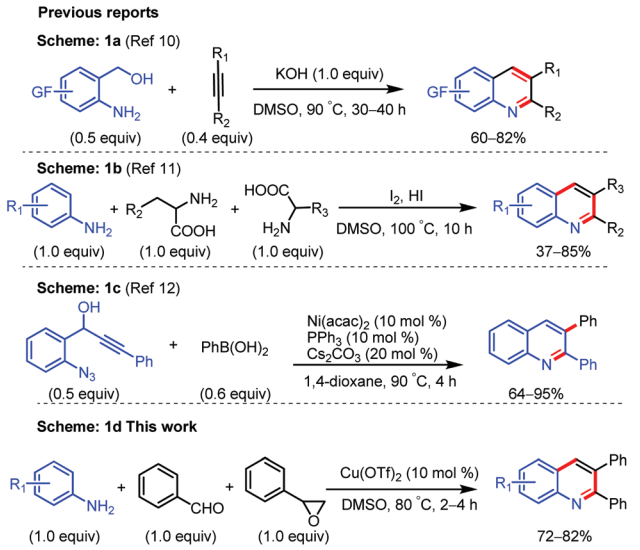


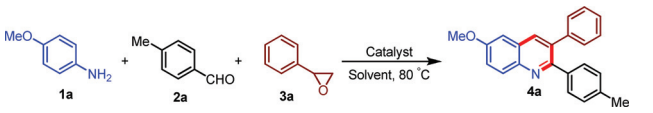
Scheme 1 Previous methods for the synthesis of 2,3-diarylquinolines and present work.

approaches.[14b–d] We report herein a copper(II) triflate catalyzed three-component reaction of aryl amines, aryl aldehydes and styrene oxides, which provides an alternative route to synthesize the 2,3-diarylquinoline skeletons under mild reaction conditions (Scheme 1d). To the best of our knowledge, copper (II) triflate catalyzed multicomponent reactions of aryl amines, aryl aldehydes and styrene oxides are not known so far.

Results and discussion

To find out the optimum reaction conditions, we have chosen *p*-anisidine (**1a**, 1.0 mmol), *p*-tolualdehyde (**2a**, 1.0 mmol) and styrene oxide (**3a**, 1.0 mmol) as the model substrates shown in Table 1. At first, the reactions were carried out without a catalyst in DMSO at room temperature as well as heating at 80 °C (Table 1, entries 1 & 2). No desired product was obtained in both the cases other than imine formation. Then, a similar reaction was performed in the presence of 5 mol% of $Cu(OTf)_2$ at room temperature and no reaction took place (Table 1, entry 3). Interestingly, an identical reaction provided **4a** in 31% yield upon heating at 80 °C (Table 1, entry 4). From the spectral analysis of compound **4a** by IR, ^{1}H NMR, ^{13}C NMR and HRMS, it was found to be 6-methoxy-3-phenyl-2-*p*-tolylquinoline **4a**. Next, we tried to improve the yield of the desired product **4a** by screening the reaction with different parameters such as catalyst loadings, and changing catalysts and solvents. Therefore, firstly, we tested the effect of loading of the catalyst and we carried out the model reaction in the presence of 10 mol% of $Cu(OTf)_2$ (Table 1, entry 5). It was noted that the reaction proceeded faster and it was completed in 2 h. The yield of the product **4a** also improved significantly. When the catalyst loading was increased from 10 to 15 mol% of $Cu(OTf)_2$, the yield of the product **4a** (Table 1, entry 6) decreased. In order to

Table 1 Optimization of reaction conditions[a,b]



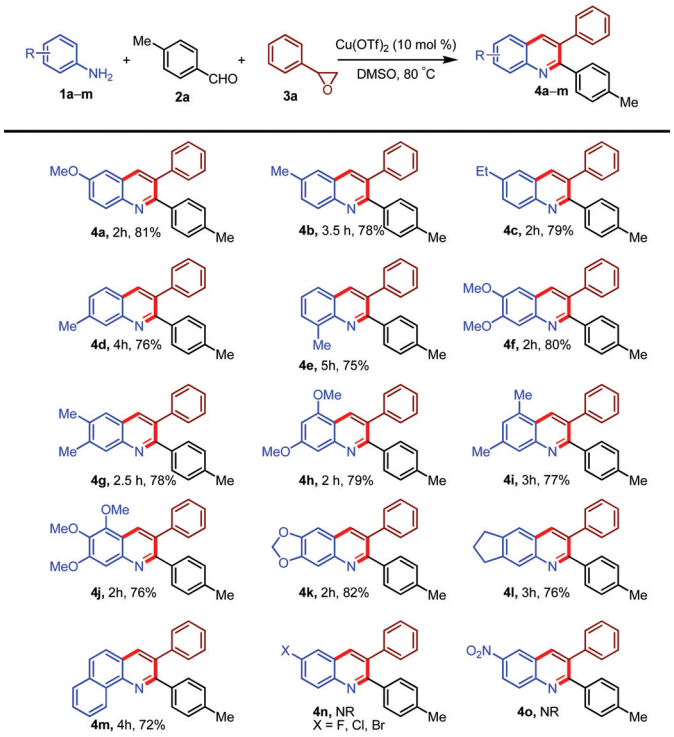
Entry	Catalyst	mol%	Solvent	Time	Yield **4a** [b] (%)
1[c]	—	—	DMSO	4 h	NR
2	—	—	DMSO	4 h	NR
3[c]	$Cu(OTf)_2$	5	DMSO	4 h	NR
4	$Cu(OTf)_2$	5	DMSO	4 h	31
5	**$Cu(OTf)_2$**	**10**	**DMSO**	**2 h**	**81**
6	$Cu(OTf)_2$	15	DMSO	2 h	72
7	$Bi(OTf)_3$	10	DMSO	2 h	36
8	$Sc(OTf)_3$	10	DMSO	2 h	28
9	$Yb(OTf)_3$	10	DMSO	2 h	25
10	AgOTf	10	DMSO	2 h	30
11	$Cu(OTf)_2$	10	Dioxane	2 h	30
12	$Cu(OTf)_2$	10	$(CH_2Cl)_2$	2 h	35
13	$Cu(OTf)_2$	10	THF	2 h	26
14	$Cu(OTf)_2$	10	DMF	2 h	NR
15	$Cu(OTf)_2$	10	EtOH	2 h	NR
16	$Cu(OTf)_2$	10	H_2O	2 h	NR

[a] Reaction conditions: All the reactions were performed using *p*-anisidine (**1a**, 1.0 mmol), *p*-tolualdehyde (**2a**, 1.0 mmol), and styrene oxide (**3a**, 1.0 mmol) in solvent (1.0 mL) at 80 °C. [b] Isolated yield. [c] Reaction performed at room temperature. NR (no desired product).

check the efficacy of other catalysts, we screened a similar reaction with different catalysts, such as $Bi(OTf)_3$, $Sc(OTf)_3$, $Yb(OTf)_3$ and AgOTf (Table 1, entries 7–10). It was noted that none of them was found to be better than $Cu(OTf)_2$ amongst various Lewis acids. To find out the solvent effect, the same set of reactions was run in the presence of 10 mol% of $Cu(OTf)_2$ in different solvents, such as 1,4-dioxane, 1,2-dichloroethane $(CH_2Cl)_2$, tetrahydrofuran (THF), *N*,*N*-dimethylformamide (DMF), ethanol (EtOH) and water (H_2O). It was observed that these solvents gave either low yield or no reaction at all (Table 1, entries 11–16). In view of the above extensive optimization, the best reaction conditions to obtain the desired products are: 10 mol% of $Cu(OTf)_2$ as a catalyst in DMSO solvent and heating at 80 °C.

After achieving the optimized reaction conditions, we investigated the scope and applicability of the developed method by performing the reactions of various substituted anilines (**1a–m**, 1.0 mmol) with *p*-tolualdehyde (**2a**, 1.0 mmol) and styrene oxide (**3a**, 1.0 mmol), and successful results are shown in Table 2. The reaction occurred smoothly with anilines containing electron-donating groups at various positions in the aromatic ring. The reaction with anilines having the electron-donating groups at the *para* position such as 4-Me and 4-Et underwent very well and produced the corresponding products **4b** and **4c** in 78% and 79% yields, respectively. The substituent methyl group at the 3- and 2-positions of aniline also showed very good results; and the reaction underwent quickly to afford the anticipated products **4d** and **4e** in 76% and 75% yields, respectively. Similarly, the reaction of di-substituted anilines, such as 3,4-OMe, 3,4-Me, 3,5-OMe and 3,5-Me, under opti-

Table 2 The reaction of various substituted anilines **1a–m** with *p*-tolualdehyde **2a** and styrene oxide **3a** [a,b]



[a] Reaction conditions: All the reactions were carried out using substituted anilines **1a–m** (1.0 mmol), *p*-tolualdehyde **2a** (1.0 mmol), styrene oxide **3a** (1.0 mmol), $Cu(OTf)_2$ (10 mol%) and DMSO (1.0 mL) at 80 °C. [b] Isolated yield. NR (no desired product).

mized conditions provided the expected products **4e–h** in 80–77% yields. Gratifyingly, 3,4,5-OMe aniline being sterically crowded also gave the corresponding quinoline derivative in 76% yield. The fused aniline derivatives, such as **1k** 3,4-(methylenedioxy)-aniline, **1l** 5-aminoindane and **1m** 1-naphthylamine, showed good reactivity and delivered the desired structurally complex quinoline derivatives **4k–m** in 82–72% yields. We have not observed the formation of other regio-isomers of compounds of **4d**, **4f**, **4g**, **4k** and **4l** due to the steric hindrance of the methyl group at the 3-position of the aniline moiety as well as more electron density at the *para* position with respect to the methyl or OMe group due to the *+I* effect.

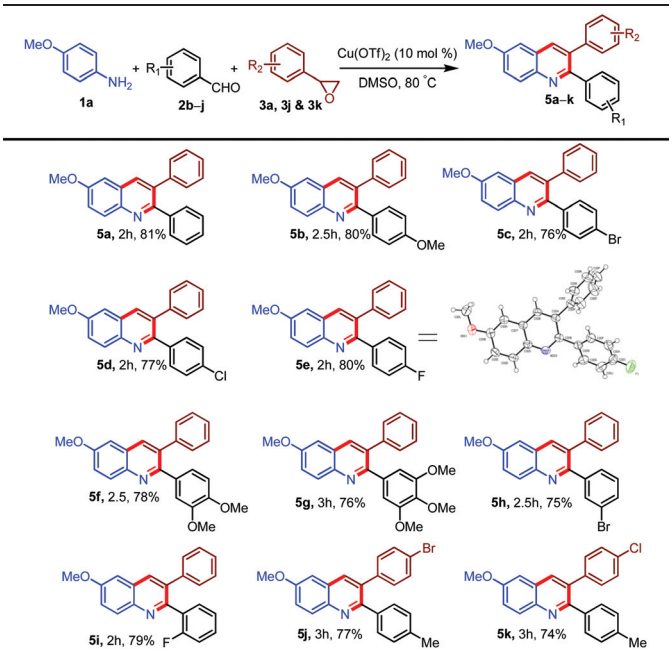
Unfortunately, the aniline having electron-withdrawing substituents such as F and NO_2 did not provide the corresponding products **4n** and **4o** as expected under identical reaction conditions because of less electron density at the *ortho*-position with respect to the amine group. In the case of Cl and Br substituents also, the reaction failed because it enhanced the electron density at the 4-position due to delocalization of electrons on halogen atoms rather than increasing at the 2-position with respect to the amino group.

Inspired by the successful results described above, we extended the scope and generality of this strategy further with *p*-anisidine (**1a**, 1.0 mmol) and various benzaldehydes (**2**, 1.0 mmol) and styrene oxides (**3**, 1.0 mmol) under the optimized conditions; their successful results are presented in Table 3. It is noteworthy that electron-donating and electron-withdrawing substituents present on benzaldehyde were well tolerated. The reaction of **1a** *p*-anisidine with **2b** simple benzaldehyde and **3a** styrene oxide proceeded well to furnish the desired product **5a** in 81% yield. Similarly, benzaldehydes having substituents at the *p*-position, such as 4-OMe, 4-Br, 4-Cl and 4-F, showed good reactivity under optimized conditions, and the reactions proceeded smoothly to provide the expected products **5b–e** in excellent yields. Likewise, 2,4-OMe and 3,4,5-OMe benzaldehydes upon reaction with *p*-anisidine **1a** and styrene oxide **3a** gave the corresponding products **5f** and **5g** in 78% and 76% yields, respectively. The 3-Br and 2-F benzaldehydes were also found to be reactive enough and they delivered the desired products **5h** and **5i** in 75% and 79% yields, respectively. Thereafter, the reaction of 4-Br and 4-Cl styrene oxides with *p*-anisidine **1a** and *p*-tolualdehyde **3a** successfully afforded the expected products **5j** and **5k** in 77% and 74% yields, respectively.

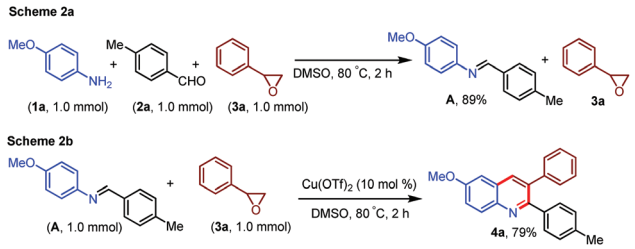
All the synthesized compounds were characterised by IR, ^1H NMR, ^{13}C NMR and HRMS analyses. In addition, the structure of compound **5e** was further established using single X-ray crystallographic data (see the ESI†).

In order to gain insights into the reaction mechanism, we performed control experiments (Scheme 2). We carried out the

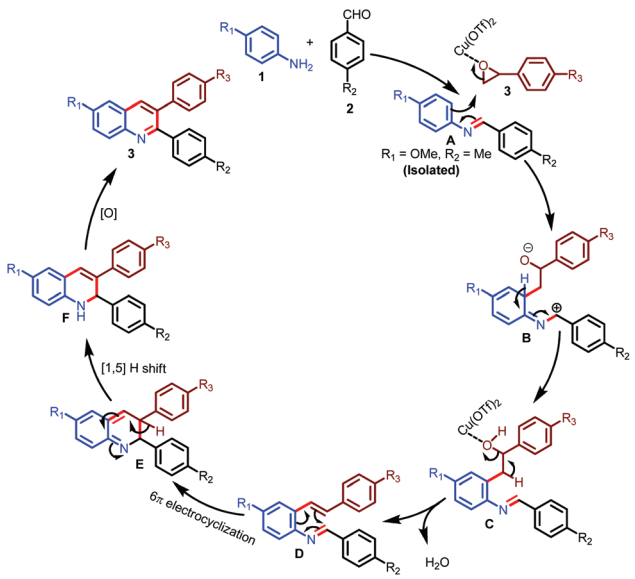
Table 3 The reaction of *p*-anisidine **1a** with various benzaldehydes (**2b–j**) and styrene oxide (**3a**, **3j** & **3k**) derivatives [a,b]



[a] Reaction conditions: All the reactions were carried out using *p*-anisidine **1a** (1.0 mmol), benzaldehydes **2b–j** (1.0 mmol), styrene oxides **3a**, **3i** & **3k** (1.0 mmol), $Cu(OTf)_2$ (10 mol%), and DMSO (1.0 mL) at 80 °C. [b] Isolated yield.



Scheme 2 Control experiments.



Scheme 3 The plausible mechanism for the formation of products.

first experiment using *p*-anisidine **1a**, *p*-tolualdehyde **2a** and styrene oxide **3a**. After stirring the reaction mixture for 2 h, intermediate **A** (Schiff's base) was isolated in 89% yield and characterized by ^{1}H NMR, ^{13}C NMR and HRMS (Scheme 2a). Thereafter, we performed another experiment using intermediate **A** and styrene oxide **3a** under standard conditions (Scheme 2b). The reaction was completed in 2 h and the expected product **4a** was obtained in 79% yield. From this observation, the formation of Schiff's base and its involvement in the reaction mechanism are confirmed.

From the observation of control experiments, the plausible mechanism for the formation of 2,3-diarylquinoline derivatives is shown in Scheme 3. At first, aryl amine **1** reacts with aryl aldehyde **2** to give an intermediate **A** (Schiff's base),[15] which then reacts with styrene oxide **3** to give the intermediate **B**, which upon aromatization provides **C**. The intermediate **C** was detected by mass spectrometry. Elimination of water from the intermediate **C** forms **D**, which undergoes 6π-electrocyclic ring closure[16] to produce intermediate **E**. The intermediate **E** involves a [1, 5] H shift[16b] to give dihydroquinoline **F** followed by aerial oxidation[16b] providing the desired quinoline **3**.

Conclusion

We have developed an efficient and straightforward novel route for the synthesis of a wide range of 2,3-diarylquinoline derivatives of biological importance *via* copper(II) triflate catalyzed multicomponent reaction using readily available aryl amines, aryl aldehydes and styrene oxides at 80 °C. The salient features of this methodology are its cost effective use, high atom economy, high regioselectivity, convenient use, shorter reaction time, consecutive one C–N and two C–C bond formation and broad substrate scope with good yield. Further study in this area is under way in our laboratory.

Experimental

General information and methods

Melting points were determined on a melting point apparatus (Buchi-540). ^{1}H and ^{13}C NMR spectra were recorded on 400 & 600 MHz and 100 & 150 MHz NMR spectrometers (Bruker), respectively. TMS was used as an internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR spectra are reported in the order: multiplicity, coupling constant (J value) in Hertz (Hz) and no. of protons; signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet) and bs (broad). IR spectra were recorded on an IR spectrophotometer (PerkinElmer). HRMS spectra were recorded using a TOF mass analyzer.

General procedure for the synthesis of 2,3-diarylquinoline derivatives

Aryl amine (**1**, 1.0 mmol), aryl aldehyde (**2**, 1.0 mmol) and styrene oxide (**3**, 1.0 mmol) were taken in dimethyl sulfoxide solvent (1.0 mL) in a round-bottomed flask (10 mL). To the reaction mixture, copper(II) triflate (10 mol%, 36 mg) was added. The resulting reaction mixture was kept under stirring in an oil-bath at 80 °C. The reaction progress was checked by TLC. After the completion of the reaction, the mixture was cooled to room temperature. To extract the product, EtOAc (3 × 5 mL) was added to the reaction mixture. The combined organic layer was washed with water (2 × 5 mL) followed by brine solution (5 mL) and dried over anhydrous Na_2SO_4. The solvent was removed in a rotary evaporator and the crude residue was purified using silica gel (60–120 mesh) column chromatography.

6-Methoxy-3-phenyl-2-*p*-tolylquinoline (4a). (263 mg, 81%, yellowish semi-liquid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.08 (d, J = 9.2 Hz, 1H), 8.04 (s, 1H), 7.37 (dd, J = 9.2, 2.8 Hz, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.26 (m, 5H), 7.11 (d, J = 2.7 Hz, 1H), 7.06 (d, J = 7.9 Hz, 2H), 3.95 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.1, 156.1, 143.7, 140.5, 137.8, 137.7, 136.6, 134.9, 131.0, 130.1, 129.9, 128.8, 128.4, 128.3, 127.2, 122.5, 105.0, 55.8, 21.4; ν_{max}/cm^{-1} 3025 (Ar–H), 2923 (C–H), 1622 (C=C), 1232 (C–O); HRMS (ESI) Calcd for $C_{23}H_{20}NO$ 326.1545 (M + H^{+}); Found 326.1571.

6-Methyl-3-phenyl-2-*p*-tolylquinoline (4b). (242 mg, 78%, yellow liquid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.01 (d, J = 8.6 Hz, 1H), 7.98 (s, 1H), 7.53 (s, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.23–7.17 (m, 5H), 6.99 (d, J = 7.9 Hz, 2H), 2.48 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 157.7, 146.1, 140.5, 137.9, 137.7, 137.2, 136.7, 134.7, 132.1, 130.1, 129.9, 129.2, 128.8, 128.4, 127.4, 127.2, 126.4, 21.9, 21.5; ν_{max}/cm^{-1} 3027 (Ar–H), 2924 (C–H), 1600 (C=C); HRMS (ESI) Calcd for $C_{23}H_{20}N$ 310.1596 (M + H$^+$); Found 310.1589.

6-Ethyl-3-phenyl-2-*p*-tolylquinoline (4c). (255 mg, 79%, dark brown liquid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.02 (d, J = 8.6 Hz, 1H), 7.98 (s, 1H), 7.52 (s, 1H), 7.49 (d, J = 8.6 Hz, 1H), 7.24 (d, J = 8.1 Hz, 2H), 7.18 (ddd, J = 13.9, 6.5, 3.3 Hz, 5H), 6.97 (d, J = 7.9 Hz, 2H), 2.75 (q, J = 7.6 Hz, 2H), 2.22 (s, 3H), 1.25 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 157.7, 146.3, 142.9, 140.6, 137.8, 137.8, 137.3, 134.6, 131.0, 130.1, 129.9, 129.9, 129.3, 128.8, 128.3, 127.2, 125.1, 76.9, 29.1, 21.4, 15.6; ν_{max}/cm^{-1} 3032 (Ar–H), 2964 (C–H), 1600 (C=C); HRMS (ESI) Calcd for $C_{24}H_{22}N$ 324.1752 (M + H$^+$); Found 324.1775.

7-Methyl-3-phenyl-2-*p*-tolylquinoline (4d). (234 mg, 76%, yellow liquid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.09 (s, 1H), 7.97 (s, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.32–7.24 (m, 5H), 7.07 (d, J = 8.1 Hz, 2H), 2.58 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.5, 147.7, 140.6, 140.0, 137.9, 137.9, 137.5, 133.9, 130.1, 129.9, 129.1, 128.8, 128.6, 128.4, 127.3, 127.2, 125.4, 22.1, 21.5; ν_{max}/cm^{-1} 3034 (Ar–H), 2922 (C–H), 1601 (C=C); HRMS (ESI) Calcd for $C_{23}H_{20}N$ 310.1596 (M + H$^+$); Found 310.1620.

8-Methyl-3-phenyl-2-*p*-tolylquinoline (4e). (232 mg, 75%, greenish liquid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.10 (s, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 6.9 Hz, 1H), 7.46–7.40 (m, 3H), 7.36–7.28 (m, 5H), 7.08 (d, J = 7.9 Hz, 2H), 2.88 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 156.74, 146.5, 140.8, 138.0, 138.0, 137.6, 134.2, 130.5, 130.1, 129.9, 129.71, 128.7, 128.5, 127.2, 127.2, 126.5, 125.5, 21.5, 18.1; ν_{max}/cm^{-1} 3034 (Ar–H), 2919 (C–H), 1600 (C=C); HRMS (ESI) Calcd for $C_{23}H_{20}N$ 310.1596 (M + H$^+$); Found 310.1620.

6,7-Dimethoxy-3-phenyl-2-*p*-tolylquinoline (4f). (285 mg, 80%, white solid); mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 7.90 (s, 1H), 7.45 (s, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.20–7.14 (m, 5H), 6.98 (d, J = 9.8 Hz, 3H), 3.96 (s, 3H), 3.93 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 156.2, 152.9, 150.2, 144.3, 140.6, 137.7, 136.3, 132.9, 130.1, 129.9, 128.8, 128.3, 127.1, 122.9, 108.1, 104.9, 56.4, 56.3, 21.4; ν_{max}/cm^{-1} 3012 (Ar–H), 2924 (C–H), 1619 (C=C), 1231 (C–O); HRMS (ESI) Calcd for $C_{24}H_{22}NO_2$ 356.1651 (M + H$^+$); Found 356.1650.

6,7-Dimethyl-3-phenyl-2-*p*-tolylquinoline (4g). (252 mg, 78%, yellowish semi-solid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 7.95 (s, 1H), 7.90 (s, 1H), 7.51 (s, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.22–7.16 (m, 5H), 6.99 (d, J = 7.9 Hz, 2H), 2.42 (s, 3H), 2.39 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 157.5, 146.6, 140.7, 140.1, 137.8, 136.9, 136.8, 133.9, 130.2, 129.9, 128.8, 128.4, 127.1, 126.8, 126.0, 21.5, 20.7, 20.3; ν_{max}/cm^{-1} 3029 (Ar–H), 2921 (C–H), 1599 (C=C); HRMS (ESI) Calcd for $C_{24}H_{22}N$ 324.1752 (M + H$^+$); Found 324.1750.

5,7-Dimethoxy-3-phenyl-2-*p*-tolylquinoline (4h). (281 mg, 79%, brown semi-solid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.35 (s, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.21–7.13 (m, 5H), 7.05 (s, 1H), 6.98 (d, J = 7.9 Hz, 2H), 6.44 (s, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 161.6, 158.9, 156.2, 149.5, 140.8, 137.9, 137.8, 132.8, 131.6, 130.1, 130.0, 128.8, 128.3, 126.9, 115.8, 99.8, 98.3, 55.9, 55.9, 21.4; ν_{max}/cm^{-1} 3018 (Ar–H), 2928 (C–H), 1620 (C=C), 1211 (C–O); HRMS (ESI) Calcd for $C_{24}H_{22}NO_2$ 356.1651 (M + H$^+$); Found 356.1637.

5,7-Dimethyl-3-phenyl-2-*p*-tolylquinoline (4i). (250 mg 77%, yellow solid); mp 111–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.15 (s, 1H), 7.76 (s, 1H), 7.26 (d, J = 8.1 Hz, 2H), 7.24–7.18 (m, 5H), 7.14 (s, 1H), 6.99 (d, J = 7.9 Hz, 2H), 2.59 (s, 3H), 2.45 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 157.9, 148.1, 140.9, 139.7, 137.9, 137.8, 134.3, 134.2, 133.4, 130.2, 130.0, 129.6, 128.8, 128.4, 127.2, 126.7, 124.7, 22.1, 21.4, 18.7; ν_{max}/cm^{-1} 3032 (Ar–H), 2922 (C–H), 1601 (C=C); HRMS (ESI) Calcd for $C_{24}H_{22}N$ 324.1752 (M + H$^+$); Found 324.1752.

5,6,7-Trimethoxy-3-phenyl-2-*p*-tolylquinoline (4j). (281 mg, 76%, brown semi-solid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.24 (s, 1H), 7.27 (s, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.17–7.13 (m, 5H), 6.95 (d, J = 7.9 Hz, 2H), 3.97 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, Me_4Si) δ 157.7, 156.1, 146.9, 145.1, 140.9, 140.6, 137.7, 137.7, 132.3, 132.1, 129.9, 129.9, 128.7, 128.2, 126.9, 118.2, 104.2, 61.7, 61.3, 56.2, 21.3; ν_{max}/cm^{-1} 3024 (Ar–H), 2935 (C–H), 1610 (C=C), 1225 (C–O); HRMS (ESI) Calcd for $C_{25}H_{24}NO_3$ 386.1756 (M + H$^+$); Found 386.1750.

7-Phenyl-6-*p*-tolyl-[1,3]dioxolo[4,5-*g*]quinoline (4k). (278 mg, 82%, dark brown semi-solid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 7.86 (s, 1H), 7.40 (s, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.21–7.12 (m, 5H), 6.98 (d, J = 9.8 Hz, 3H), 6.02 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, Me_4Si) δ 156.1, 150.9, 148.1, 145.6, 140.4, 137.7, 137.6, 136.8, 132.9, 130.0, 129.9, 128.8, 128.4, 127.1, 124.2, 105.9, 102.5, 101.8, 21.4; ν_{max}/cm^{-1} 3032 (Ar–H), 2913 (C–H), 1611 (C=C), 1220 (C–O); HRMS (ESI) Calcd for $C_{23}H_{18}NO_2$ 340.1338 (M + H$^+$); Found 386.1365.

3-Phenyl-2-*p*-tolyl-7,8-dihydro-6*H*-cyclopenta[*g*]quinoline (4l). (255 mg, 76%, yellow solid); mp 110–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 7.97 (s, 1H), 7.92 (s, 1H), 7.55 (s, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.22–7.17 (m, 5H), 6.99 (d, J = 7.9 Hz, 2H), 3.07–2.98 (m, 4H), 2.24 (s, 3H), 2.10 (quint, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 157.3, 148.0, 147.3, 144.5, 140.7, 137.7, 137.4, 133.6, 130.1, 129.9, 128.8, 128.4, 128.3, 127.1, 126.5, 123.7, 121.5, 33.2, 32.7, 26.4, 21.4; ν_{max}/cm^{-1} 3029 (Ar–H), 2948 (C–H), 1599 (C=C); HRMS (ESI) Calcd for $C_{25}H_{22}N$ 336.1752 (M + H$^+$); Found 336.1752.

3-Phenyl-2-*p*-tolylbenzo[*h*]quinoline (4m). (249 mg, 72%, white solid); mp = 140–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.16 (s, 1H), 7.92 (d, J = 7.1 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.74–7.69 (m, 3H), 7.51 (d, J = 8.1 Hz, 2H), 7.34 (s, 4H), 7.12 (d, J = 7.9 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$, Me_4Si) δ 156.3, 145.5, 140.7, 138.0, 137.9, 134.9, 133.9, 131.8, 130.6, 129.9, 128.8, 128.5, 128.3, 127.9, 127.6, 127.3, 127.1, 125.2, 125.2, 125.1, 21.5; ν_{max}/cm^{-1} 3041 (Ar–H), 2923 (C–H), 1590 (C=C); HRMS (ESI) Calcd for $C_{26}H_{20}N$ 346.1596 ($M + H^+$); Found 346.1609.

6-Methoxy-2,3-diphenylquinoline (5a). (311 mg, 81%, dark solid); mp 123–125 °C; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.10 (d, J = 9.2 Hz, 1H), 8.06 (s, 1H), 7.43–7.37 (m, 3H), 7.28–7.25 (m, 8H), 7.12 (d, J = 2.7 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.2, 156.1, 143.6, 140.7, 140.3, 136.6, 134.9, 131.1, 130.2, 129.9, 128.4, 128.4, 128.1, 127.9, 127.3, 122.6, 105.1, 55.8; ν_{max}/cm^{-1} 3059 (Ar–H), 2834 (C–H), 1623 (C=C), 1233 (C–O); HRMS (ESI) Calcd for $C_{22}H_{18}NO$ 312.1388 ($M + H^+$); Found 312.1411.

6-Methoxy-2-(4-methoxyphenyl)-3-phenylquinoline (5b). (274 mg, 80%, brown liquid); ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.06 (d, J = 9.2 Hz, 1H), 7.97 (s, 1H), 7.31 (dd, J = 8.9, 4.0 Hz, 3H), 7.23 (t, J = 5.0 Hz, 3H), 7.18 (t, J = 3.8 Hz, 2H), 7.04 (d, J = 2.7 Hz, 1H), 6.72 (d, J = 8.7 Hz, 2H), 3.88 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 159.8, 158.2, 155.5, 143.2, 140.4, 137.1, 134.9, 131.7, 130.6, 129.9, 129.5, 128.5, 128.3, 127.4, 122.7, 113.6, 105.1, 55.8, 55.4; ν_{max}/cm^{-1} 3018 (Ar–H), 2929 (C–H), 1619 (C=C), 1232 (C–O); HRMS (ESI) Calcd for $C_{23}H_{20}NO_2$ 342.1494 ($M + H^+$); Found 342.1542.

2-(4-Bromophenyl)-6-methoxy-3-phenylquinoline (5c). (296 mg, 76%, brown solid); mp 142–144 °C; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.07 (d, J = 8.8 Hz, 2H), 7.40 (dd, J = 8.8, 2.3 Hz, 3H), 7.33–7.30 (m, 5H), 7.23 (dd, J = 6.6, 3.0 Hz, 2H), 7.12 (d, J = 2.8 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.4, 154.7, 143.7, 140.0, 139.6, 136.8, 134.8, 131.9, 131.3, 131.1, 129.9, 128.6, 128.5, 127.6, 122.8, 122.5, 105.0, 55.8; ν_{max}/cm^{-1} 3021 (Ar–H), 2925 (C–H), 1622 (C=C), 1233 (C–O); HRMS (ESI) Calcd for $C_{22}H_{17}BrNO$ 390.0494 ($M + H^+$); Found 390.0483.

2-(4-Chlorophenyl)-6-methoxy-3-phenylquinoline (5d). (266 mg, 77%, brown solid); mp 148–150 °C; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.07 (d, J = 8.9 Hz, 2H), 7.41–7.38 (m, 1H), 7.38–7.36 (m, 2H), 7.32 (dd, J = 5.0, 1.8 Hz, 3H), 7.26–7.22 (m, 4H), 7.12 (d, J = 2.7 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.4, 154.7, 143.7, 140.0, 139.2, 136.8, 134.8, 134.1, 131.6, 131.0, 129.9, 128.6, 128.5, 128.3, 127.5, 122.8, 104.9, 55.8; ν_{max}/cm^{-1} 3025 (Ar–H), 2926 (C–H), 1623 (C=C), 1232 (C–O); HRMS (ESI) Calcd for $C_{22}H_{17}ClNO$ 346.0999 ($M + H^+$); Found 346.1026.

2-(4-Fluorophenyl)-6-methoxy-3-phenylquinoline (5e). (266 mg, 80%, brown solid); mp 95–97 °C; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.07 (d, J = 9.9 Hz, 2H), 7.43–7.37 (m, 3H), 7.31 (dd, J = 5.0, 1.8 Hz, 3H), 7.23 (dd, J = 6.6, 3.1 Hz, 2H), 7.12 (d, J = 2.8 Hz, 1H), 6.95 (t, J = 8.8 Hz, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 162.8 (d, $^1J_{C-F}$ = 246 Hz), 158.3, 155.0, 143.7, 140.2, 136.7 (d, $^3J_{C-F}$ = 5 Hz), 134.8, 132.1, 131.98, 131.0, 129.9, 128.5, 128.4, 127.5, 122.7, 115.1 ($^2J_{C-F}$ = 21 Hz), 105.0, 55.82; ν_{max}/cm^{-1} 3022 (Ar–H), 2926 (C–H), 1623 (C=C), 1230 (C–O); HRMS (ESI) Calcd for $C_{22}H_{17}FNO$ 330.1294 ($M + H^+$); Found 330.1321.

2-(3,4-Dimethoxyphenyl)-6-methoxy-3-phenylquinoline (5f). (292 mg, 78%, dark brown liquid); ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.08 (d, J = 9.2 Hz, 1H), 8.04 (s, 1H), 7.38 (dd, J = 9.2, 2.8 Hz, 1H), 7.29 (dt, J = 7.2, 4.8 Hz, 5H), 7.11 (dd, J = 8.1, 2.2 Hz, 2H), 6.89 (d, J = 2.0 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 3.96 (s, 3H), 3.87 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.1, 155.6, 149.1, 148.3, 143.7, 140.8, 136.7, 134.9, 133.2, 131.0, 129.9, 128.5, 128.2, 127.3, 123.0, 122.5, 113.8, 110.9, 105.1, 56.1, 55.8, 55.8; ν_{max}/cm^{-1} 3011 (Ar–H), 2929 (C–H), 1623 (C=C), 1233 (C–O); HRMS (ESI) Calcd for $C_{24}H_{22}NO_3$ 372.1600 ($M + H^+$); Found 372.1627.

6-Methoxy-3-phenyl-2-(3,4,5-trimethoxyphenyl)quinoline (5g). (308 mg, 76%, dark brown liquid); ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.17 (d, J = 9.0 Hz, 1H), 8.09 (s, 1H), 7.41 (dd, J = 9.2, 2.8 Hz, 1H), 7.35–7.27 (m, 5H), 7.13 (d, J = 2.7 Hz, 1H), 6.68 (s, 2H), 3.96 (s, 3H), 3.82 (s, 3H), 3.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.4, 155.44, 152.9, 140.649, 138.7, 137.0, 135.0, 130.7, 129.8, 128.6, 128.4, 127.4, 122.93, 115.1, 115.0, 108.0, 105.1, 65.4, 61.1, 56.1, 55.83; ν_{max}/cm^{-1} 3014 (Ar–H), 2934 (C–H), 1590 (C=C), 1241 (C–O); HRMS (ESI) Calcd for $C_{25}H_{24}NO_4$ 402.1705 ($M + H^+$); Found 402.1749.

2-(3-Bromophenyl)-6-methoxy-3-phenylquinoline (5h). (293 mg, 75%, brown liquid); ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.02 (s, 1H), 7.64 (s, 1H), 7.35 (dd, J = 9.1, 2.9 Hz, 2H), 7.27–7.23 (m, 3H), 7.19–7.15 (m, 4H), 7.06 (d, J = 2.7 Hz, 1H), 7.01 (t, J = 7.9 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.6, 154.2, 143.4, 139.7, 137.0, 134.9, 133.2, 131.1, 130.9, 129.9, 129.4, 129.0, 128.7, 128.6, 127.7, 123.1, 122.4, 105.0, 55.8; ν_{max}/cm^{-1} 3066 (Ar–H), 2929 (C–H), 1622 (C=C), 1245 (C–O); HRMS (ESI) Calcd for $C_{22}H_{17}BrNO$ 390.0494 ($M + H^+$); Found 390.0510.

2-(2-Fluorophenyl)-6-methoxy-3-phenylquinoline (5i). (260 mg, 79%, black solid); mp 84–86 °C; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.05 (d, J = 9.3 Hz, 1H), 8.02 (s, 1H), 7.46 (td, J = 7.4, 1.8 Hz, 1H), 7.33 (dd, J = 9.2, 2.8 Hz, 1H), 7.23–7.14 (m, 6H), 7.11 (dd, J = 7.5, 1.0 Hz, 1H), 7.08 (t, J = 2.7 Hz, 1H), 6.80 (t, J = 8.7 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 159.9 (d, $^1J_{C-F}$ = 247 Hz), 158.5, 151.8, 143.3, 139.6, 139.6, 136.2, 135.9, 131.9 (d, $^3J_{C-F}$ = 3 Hz), 130.9, 130.3 (d, $^3J_{C-F}$ = 8 Hz), 129.3, 128.9, 128.2, 127.4, 124.4 (d, $^3J_{C-F}$ = 3 Hz), 122.8, 115.7 (d, $^2J_{C-F}$ = 21 Hz), 105.1, 55.8; ν_{max}/cm^{-1} 3028 (Ar–H), 2920 (C–H), 1622 (C=C), 1232 (C–O); HRMS (ESI) Calcd for $C_{22}H_{17}FNO$ 330.1294 ($M + H^+$); Found 330.1322.

3-(4-Bromophenyl)-6-methoxy-2-*p*-tolylquinoline (5j). (312 mg, 77%, brown liquid); ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.07 (d, J = 9.2 Hz, 1H), 8.01 (s, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.39 (dd, J = 9.2, 2.8 Hz, 1H), 7.30 (d, J = 8.1 Hz, 2H), 7.15–7.06 (m, 5H), 3.95 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.2, 155.8, 143.8, 139.5, 137.9, 137.5, 136.5, 133.7, 131.8, 131.6, 131.5, 131.1, 130.0, 129.0, 122.8, 121.6, 104.9, 55.8, 21.5; ν_{max}/cm^{-1} 3022 (Ar–H), 2924 (C–H), 1620 (C=C), 1241 (C–O); HRMS (ESI) Calcd for $C_{23}H_{19}BrNO$ 404.0650 ($M + H^+$); Found 404.0670.

3-(4-Chlorophenyl)-6-methoxy-2-*p*-tolylquinoline (5k). (281 mg, 78%, brown liquid); ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.08 (d, J = 9.2 Hz, 1H), 8.01 (s, 1H), 7.39 (dd, J = 9.2,

2.7 Hz, 1H), 7.28 (dd, J = 9.9, 8.6 Hz, 4H), 7.21–7.15 (m, 2H), 7.10 (dd, J = 8.0, 5.4 Hz, 3H), 3.95 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.2, 155.9, 143.8, 139.0, 137.9, 137.5, 136.5, 133.7, 133.4, 131.2, 131.1, 130.0, 129.0, 128.6, 128.2, 122.8, 104.9, 55.8, 21.5; ν_{max}/cm^{-1} 3014 (Ar–H), 2929 (C–H), 1623 (C=C), 1222 (C–O); HRMS (ESI) Calcd for $C_{23}H_{19}ClNO$ 360.1155 (M + H$^+$); Found 360.1167.

(*E*)-4-Methoxy-*N*-(4-methylbenzylidene)aniline (A).[15a] (200 mg, 89%, gray solid); ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.42 (s, 1H), 7.76 (d, J = 8.1 Hz, 2H), 7.28–7.19 (m, 4H), 6.91 (d, J = 8.9 Hz, 2H), 3.80 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 158.59, 158.31, 145.29, 141.60, 134.08, 129.63, 128.76, 122.32, 114.54, 77.55, 77.23, 76.91, 55.63, 21.74; HRMS (ESI) Calcd for $C_{15}H_{16}NO$ 226.1236 (M + H$^+$); Found 226.1237.

Conflicts of interest

There are no conflicts to declare.

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