Monatsh Chem (2012) 143:471–478
DOI 10.1007/s00706-011-0590-7

ORIGINAL PAPER

Facile one-pot synthesis of polysubstituted quinolines under solvent-free conditions using sulfamic acid as a reusable catalyst

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Received: 14 July 2010 / Accepted: 15 July 2011 / Published online: 19 August 2011

Abstract A facile one-pot synthesis of polysubstituted quinoline derivatives has been demonstrated by using sulfamic acid as a reusable catalyst under solvent-free conditions. The synthetic method provides the basis and advantages of a simple experimental procedure and easy recovery and reuse of catalyst, which makes it a highly practical and environmentally benign pathway for the synthesis of polysubstituted quinolines. Interestingly, this one-pot synthesis could produce the products regioselectively in the presence of dis-symmetrical arylamines.

Keywords Multicomponent reaction · Heterocylces · Reusable sulfamic acid catalyst · Solvent-free conditions · Eliminations and oxidations

Introduction

Quinoline and its analogues represent a very important class of nitrogen-containing heterocycles because of their wide spectrum of biological and pharmaceutical activities such as anti-malaria [1], anti-leishmania [2], anti-bacteria [3], anti-asthma [4], anti-inflammation [5], anti-hypertension [6], tyrokinase inhibitor [7], histamine H_3 receptor inverse agonists [8], and therapeutic agents for estrogen-dependent diseases [9]. In addition, quinoline derivatives were widely employed as key intermediates for the manufacturing of functionalized materials [10–12] and chemosensors [13]. Considering these significant properties and functions, the development of effective methods to construct functionalized quinolines has been attracting great attention. Further, the classical reactions, such as Skraup [14], Friedlander [15], Combes [16], and Doebner-Von Miller reactions [17], were reported over a century ago, and additionally remarkable new protocols were also extensively studied by providing new access to functionalized quinolines in recent years, for example, involving the cyclization reactions from *ortho*-nitrogen-containing substrates [18, 19], cascade multicomponent reactions [20, 21], imino Diels-Alder reactions (Povarov-type reaction) [22], and condensation-cyclization reactions from *o*-haloacetophenones [23]. However, many of these synthetic methodologies still suffer from various drawbacks such as complicated reaction conditions, lack of readily available starting materials, requirement of multi-step processes, or excessive use of reagents leading to tedious laboratory procedures.

It was noteworthy that the cross-coupling reactions between aliphatic aldehydes and imines provided easier pathways for the synthesis of quinoline derivatives; however, a key pretreatment step was required to form the imines originally [24, 25]. However, the condensation reaction of two molecules of aldehydes and one molecule of arylamine showed a direct approach in achieving this goal [26, 27], but the employed catalysts were generally destroyed during the workup procedures and could not be recovered or reused.

Considering the drawbacks arising from the usage of the above-mentioned methods, the search for an effective catalytic process along with eco-compatible preparation of quinolines from readily available starting materials is of great importance. In the past decade, the application of sulfamic acid (NH_2SO_3H, SA) in catalysis has attracted

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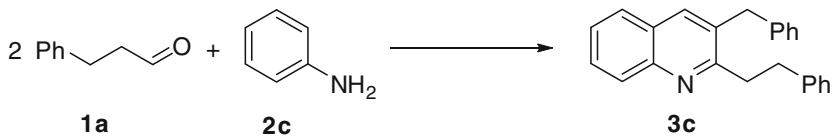
considerable attention because of its notable advantages such as being a cost-effective, non-volatile, non-hygroscopic, odorless, non-corrosive, and crystalline solid acid with outstanding physical stability [28]. We were therefore motivated to investigate its new catalytic application to the synthesis of quinoline derivatives since the construction of heterocyclic compounds is one of our major research interests [29, 30]. Hereby, we report an effective method for the synthesis of polysubstituted quinolines via a one-pot synthesis from readily available aliphatic aldehydes **1** and arylamines **2** in the presence of catalytic amounts of reusable SA catalyst under solvent-free conditions.

Results and discussion

In order to formulate a highly effective conversion system, the synthesis of 3-benzyl-2-phenethylquinoline (**3c**) from 3-phenylpropanal (**1a**, 2 mmol) and aniline (**2c**, 1 mmol) was chosen as a model reaction to evaluate the influence of different catalyst loadings and solvents. Initially, we carried out the reaction at 80 °C for 3 h under solvent-free conditions in the presence of 10 mol% of sulfamic acid catalyst, and 91% GC yield was detected (Table 1, entry 1). The usage of 9, 8, and 5 mol% of catalyst resulted in 85, 85, and 72% yield, respectively, which indicates that the decreased catalyst loadings lead to reduced yields (Table 1, entry 2). Further, an increase of catalyst loading (11 mol%) did not improve the yield significantly (Table 1, entry 3). Obviously, the use of 10 mol% of catalyst is considered to be sufficient to promote the reaction. The reaction under catalyst-free conditions failed to yield the expected product even after a prolonged reaction time spanning 24 h (Table 1, entry 4). Subsequently, we investigated the effects of several organic solvents including 1,4-dioxane, acetonitrile, ethanol, and 1,2-dichloroethane on the reactions, and 87, 72, 84, and 71% GC yield was detected respectively by employing 10 mol% of SA catalyst (Table 1, entries 5–8) at 80 °C for 3 h. The results indicate that the reaction efficiency and yields in solution are lower than those obtained under solvent-free conditions (Table 2). Thus, the optimized reaction conditions can be summarized as: 10 mol% of SA catalyst, solvent-free conditions, and 80 °C.

With the availability of the best reaction conditions in hand, we tried to recover and reuse the SA catalyst. After completion of the reaction for the first run, diethyl ether was added to the resulting mixture to separate the product. The remaining solid catalyst was recovered by filtration and reused in the next run without further purification under the optimized reaction conditions. This procedure was repeated six times, and the results are outlined in Table 1 (entry 9). The detected yields were observed to be close in proximity to the initial value in the previous four cycles, and subsequently a slight gradual decrease in the yields was observed in the two latter cycles. Hence, the catalyst could be effectively recycled for at least four times without any loss of activity.

Table 1 Screening optimized reaction conditions for the synthesis of **3c** and investigation for the reuse of catalyst



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

Entry	Catalyst loading/mol%	Solvent	Yields/%[a]
1	10	–	91
2	9, 8, 5	–	85, 85, 72
3	11	–	90
4	–	–	–[b]
5	10	1,4-Dioxane	87
6	10	MeCN	72
7	10	EtOH	84
8	10	$ClCH_2CH_2Cl$	71
9	10	–	91, 89, 88, 90, 85, 79[c]

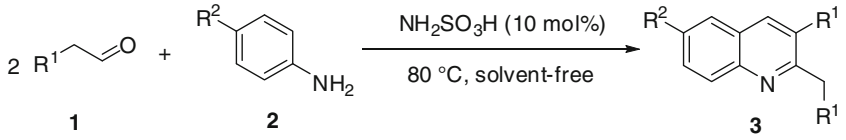
Reaction conditions: unless otherwise stated, 268 mg **1a** (2 mmol) and 93 mg aniline (**2c**, 1 mmol) along with 0.1 mmol of SA were stirred in an open Schlenk tube equipped with circulating cooling water at 80 °C for 3 h

[a] GC yields with tetradecane as internal standard

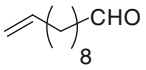
[b] The reaction was carried out for 24 h

[c] GC yields as the SA catalyst was reused for 6 cycles

Table 2 Facile one-pot synthesis of polyfunctional quinoline derivatives catalyzed by sulfamic acid under solvent-free conditions



1 **2** **3**

1a: R^1 = $PhCH_2$ **2a**: R^2 = OMe
1b: R^1 = Ph **2b**: R^2 = Me
1c: R^1 = 4-Br-C_6H_4 **2c**: R^2 = H
1d: R^1 = Et **2d**: R^2 = Br
1e =  **2e**: R^2 = Cl

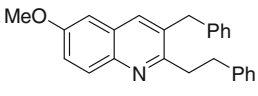
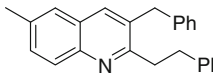
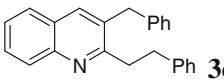
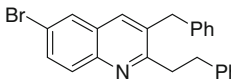
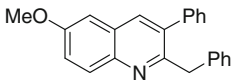
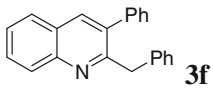
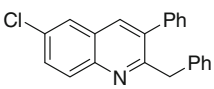
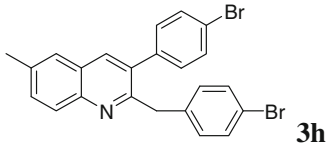
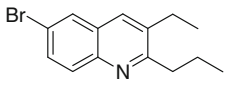
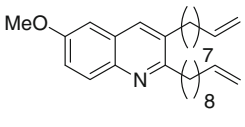
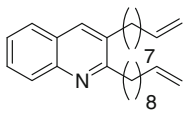
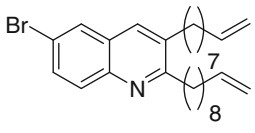
Entry	1	2	Reaction time/h	Product 3[a]	Yield/%[b]
1	**1a**	**2a**	3	 **3a** [26]	73
2	**1a**	**2b**	3	 **3b**	86
3	**1a**	**2c**	3	 **3c** [18]	83
4	**1a**	**2d**	3	 **3d**	76
5	**1b**	**2a**	3	 **3e** [21]	80
6	**1b**	**2b**	5	 **3f** [21]	78
7	**1b**	**2e**	5	 **3g**	73

Table 2 continued

Entry	1	2	Reaction time/h	Product 3[a]	Yield/%[b]
8	**1c**	**2b**	3	 **3h**	63
9	**1d**	**2d**	5	 **3i**	66
10	**1e**	**2a**	3	 **3j**	86
11	**1e**	**2c**	3	 **3k**	86
12	**1e**	**2d**	3	 **3l**	83

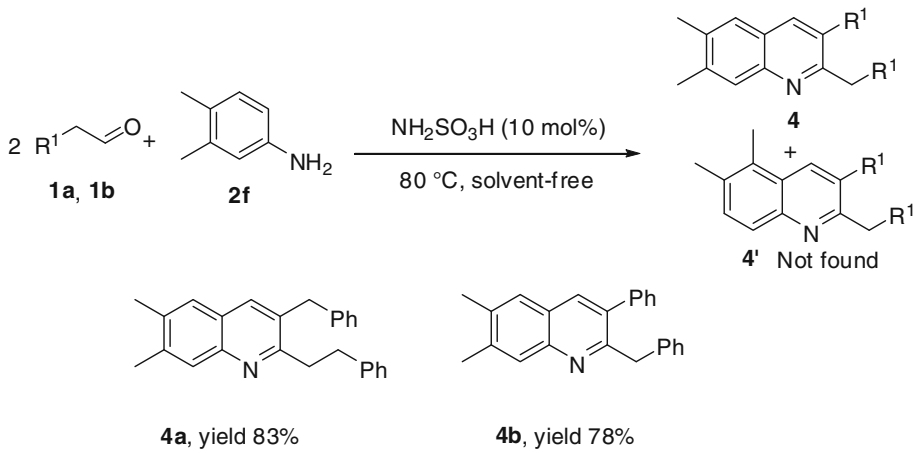
Reaction conditions: aldehyde **1** (2 mmol) and aniline derivatives **2** (1 mmol) along with 0.1 mmol of SA were stirred in an open Schlenk tube equipped with circulating cooling water at 80 °C for appropriate time

[a] Known compounds were marked with related references; the IR, ^{1}H NMR spectra were found to be identical with the ones described in the reference

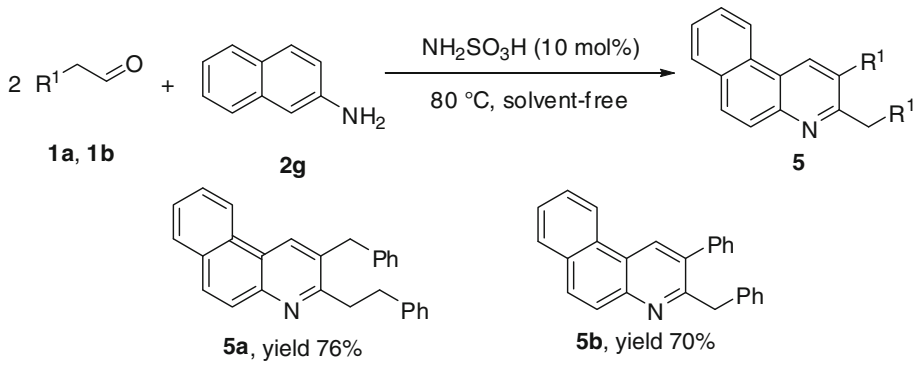
[b] Isolated yield after flash chromatography

To investigate the generality of this synthetic method under optimized reaction conditions, various aliphatic aldehydes **1** and arylamines **2** bearing weak electron withdrawing groups (such as halide) or electron releasing groups (such as CH_3, CH_3O) were employed for the quinoline synthesis. As shown in Table 2, all reactions proceeded smoothly and yielded the expected products in good to excellent isolated yields. It was found that the influence of substituents on the benzene ring of arylamines was quite effective on the reactions. The arylamines possessing electron-donating groups showed faster reactions and completed the conversion of starting materials in 3 h (Table 2, entries 1, 2, 5, 8, 10), which might be attributable to the more easy formation of imines and electrophilic attack of C(2) of arylimines to another imines (or enamines) (see the proposed mechanism, Scheme 3). As the products tolerate halides (Table 2, entries 4, 7–9, 12), they have the potential for the synthesis of molecular materials via further classical cross-coupling reactions (Table 2, entries 4, 7, 8, 10). The products **3j**, **3k**, **3l** containing two terminal vinyl groups provide the potentials in preparation of macrocyclic compounds or long chain polymers via intra- or intermolecular olefin metathesis (Table 2, entries 10, 11, 12) [31], and their arising substrate undec-10-enal (**1e**) was found to be a renewable natural resource from castor oil. Interestingly, different functional groups could be introduced into the quinoline skeleton by mediating appropriate starting materials with the current SA catalysis method (Table 2).

Scheme 1



Scheme 2



The substrate 3,4-dimethylbenzenamine (**2f**) was employed to investigate the regioselectivity of the reaction, which could lead to two possible regioisomers 4, 4′ (Scheme 1); however, the results showed that only one regioisomer **4** was obtained, and 2,3,6,7-tetrasubstituted quinoline products **4a**, **4b** were obtained in 83% and 78% isolated yields, respectively.

Similarly, the reactions of **1a**, **1b** with *β*-naphthylamine (**2g**) gave only one regioisomer **5a**, **5b** in 76 and 70% isolated yield, respectively. The results are well in agreement with the fact that the reactivity at *the* α-position is much higher than that of the *β*-position in the naphthalene moiety [32] (Scheme 2).

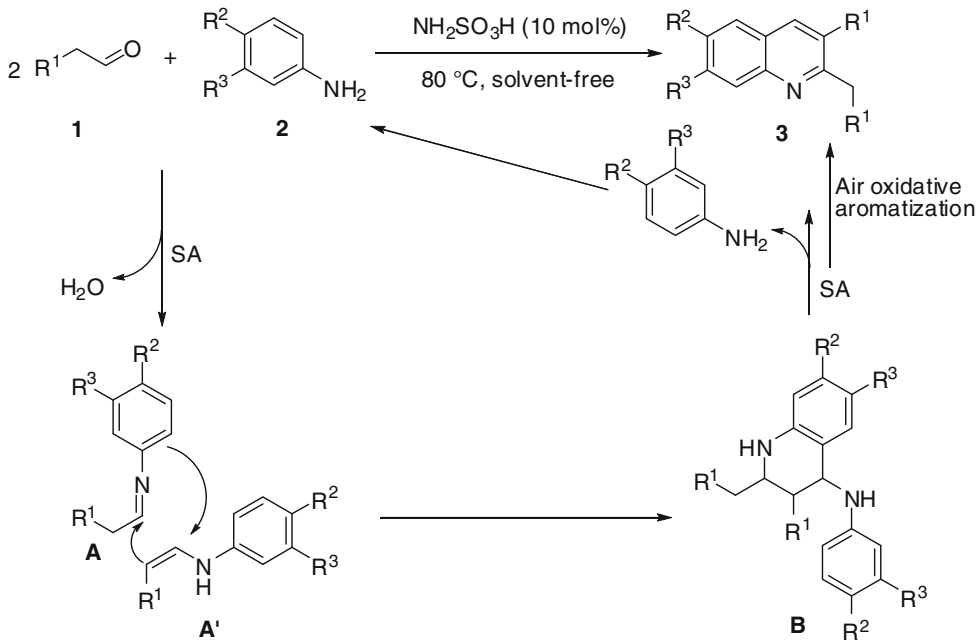
The proposed mechanism for this cyclization reaction is illustrated in Scheme 1 based on the published information [24–27, 33]. The imine **A** or its tautomer enamine **A′** is formed initially via dehydration of aliphatic aldehyde and arylamine catalyzed by the SA catalyst, then the Schiff base dimerisation and *ortho*-carbon nucleophilic addition to the enamine moiety results in tetrahydroquinoline intermediate **B**, and the final quinoline product is formed by aniline elimination and air oxidative aromatization promoted by the SA catalyst (Scheme 3). Alternatively, a Povarov reaction between imine and enol formed from aldehyde leading to the formation of quinoline could also explain the outcome of the reaction [24].

In conclusion, we have demonstrated a facile SA catalyzed method for the synthesis of polysubstituted quinoline derivatives via one-pot reactions. The method allows assembling a wide range of expected products and introducing different functional groups into the quinoline skeleton by simply mediating with the reactants. Interestingly, this one-pot synthesis could produce the products regioselectively in the presence of dis-symmetrical arylamines such as 3,4-dimethylbenzenamine and *β*-naphthylamine. The obtained products containing halides or vinyl groups have the potential for further chemical transformations. The represented simple experimental procedure along with the advantages of easy recovery and reuse of SA catalyst and solvent-free conditions makes it a highly practical and environmentally benign pathway for the synthesis of polysubstituted quinolines.

Experimental

All obtained products were characterized by melting points, ^{1}H NMR, ^{13}C NMR, infrared spectra, and low- and

Scheme 3



high-resolution mass spectra (MS and HRMS). Melting points were measured on an Electrothermal SGW-X4 microscopy digital melting point apparatus. IR spectra were recorded on a FTLA2000 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on Bruker-200 and Avance 300, chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). LRMS and HRMS were measured on a Finnigan MAT 95 spectrometer. TLC was performed using commercially prepared 100–400 mesh silica gel plates (GF254), and visualization was effected at 254 nm. All the chemical reagents were purchased from commercial sources (Alfa, Acros, Aldrich) and used without further purification.

General procedure for synthesis of the quinolines ***3a–3l, 4a, 4b, 5a, 5b***

A Schlenk tube equipped with a magnetic stirrer bar and a provision of circulating cool water was used in the experimentation. The catalyst SA (10 mg, 0.1 mmol), arylamine (1 mmol), and aldehyde (2 mmol) were introduced successively, and the resulting mixture was stirred in an open system at 80 °C for a duration of 3–5 h. TLC was used to detect the completion of the reaction. After cooling to room temperature, the reaction mixture was washed and extracted with diethyl ether (5 × 15 cm^3). The residues of the solid sulfamic acid catalyst could be recycled for the next run after removal of the solvent. The combined organic solvent was evaporated to afford the crude product, which was purified by using flash column chromatography on silica eluting with petroleum ether-ethyl acetate (30:1) to provide desired quinoline products.

3-Benzyl-6-methoxy-2-(2-phenylethyl)quinoline (**3a**) *[26]*
Yield 73%; white solid; m.p.: 136–137 °C (Ref. [26] 142–144 °C).

3-Benzyl-6-methyl-2-(2-phenylethyl)quinoline (**3b**, $C_{25}H_{23}N$)
Yield 86%; white solid; m.p.: 124–126 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.01$ (d, $J = 8.4$ Hz, 1H), 7.70 (s, 1H), 7.51–7.55 (m, 2H), 7.11–7.36 (m, 10H), 4.08 (s, 2H), 3.19–3.28 (m, 2H), 3.03–3.13 (m, 2H), 2.54 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 158.9$, 140.7, 138.1, 134.6, 134.4, 131.1, 129.8, 127.6, 127.3, 127.2, 126.8, 125.8, 125.1, 124.7, 124.6, 37.4, 36.3, 34.1, 20.2 ppm; IR (KBr): $\bar{\nu} = 3{,}021$, 2,928, 1,601, 1,493, 1,451, 1,355, 1,132, 1,031, 938 cm^{-1}; MS (EI): $m/z = 337$ [M]$^+$; HRMS (EI): 338.1902 [M + H]$^+$.

3-Benzyl-2-(2-phenylethyl)quinoline (**3c**) *[18]*
Yield 83%; white solid; m.p.: 94–97 °C.

3-Benzyl-6-bromo-2-(2-phenylethyl)quinoline (**3d**, $C_{24}H_{19}BrN$)
Yield 76%; white solid; m.p.: 89–91 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.98$ (d, $J = 9.0$ Hz, 1H), 7.89 (d, $J = 1.8$ Hz, 1H), 7.75 (dd, $J = 2.2$ Hz, 1H), 7.65 (s, 1H), 7.10–7.39 (m, 10H), 4.08 (s, 2H), 3.21–3.30 (m, 2H), 3.06–3.14 (m, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 161.7$, 145.4, 141.8, 138.8, 135.2, 133.7, 132.2, 130.4, 129.2, 129.0, 128.8, 128.6, 128.4, 128.3, 126.7, 126.0, 119.6, 38.6, 37.6, 35.1 ppm; IR (KBr): $\bar{\nu} = 3{,}025$, 2,927,

1,595, 1,494, 1,477, 1,453, 1,397, 1,059, 918 cm^{-1}; MS (EI): *m/z* = 401 $[M]^+$; HRMS (EI): 402.0842 $[M + H]^+$.

2-Benzyl-6-methoxy-3-phenylquinoline (**3e**) *[21]*
Yield 80%; light yellow oil.

2-Benzyl-3-phenylquinoline (**3f**) *[21]*
Yield 78%; colorless oil.

2-Benzyl-6-chloro-3-phenylquinoline (**3g**, $C_{22}H_{16}ClN$)
Yield 73%; colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.8 Hz, 1H), 7.89 (s, 1H), 7.66–7.80 (m, 2H), 7.13–7.44 (m, 8H), 6.94–6.98 (m, 2H), 4.34 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 160.0, 139.5, 139.4, 137.4, 136.3, 132.4, 131.0, 130.7, 129.8, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 127.9, 127.4, 126.5, 118.5, 114.4, 43.2 ppm; IR (KBr): $\bar{\nu}$ = 3,033, 2,982, 1,601, 1,498, 1,467, 1,377, 1,029, 932 cm^{-1}; MS (EI): *m/z* = 329 $[M]^+$; HRMS (EI): 330.1048 $[M + H]^+$.

2,3-Bis(4-bromobenzyl)-6-methylquinoline
(**3h**, $C_{23}H_{17}Br_2N$)
Yield 63%; white solid; m.p.: 121–123 °C; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.61–7.52 (m, 4H), 7.27 (m, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 4.23 (s, 2H), 2.57(s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 157.3, 146.3, 138.9, 138.7, 137.0, 136.9, 135.1, 132.5, 131.8, 131.6, 131.3, 130.9, 130.8, 129.1, 127.2, 126.7, 122.5, 122.5, 120.4, 42.6, 22.1 ppm; IR (KBr): $\bar{\nu}$ = 3,021, 2,981, 1,605, 1,499, 1,427, 1,376, 1,033, 933 cm^{-1}; MS (EI): *m/z* = 466 $[M + 1]^+$; HRMS (EI): 465.9804 $[M + H]^+$.

6-Bromo-3-ethyl-2-propylquinoline (**3i**, $C_{14}H_{16}BrN$)
Yield 66%; colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.87–7.91 (m, 2H), 7.77 (s, 1H), 7.64–7.70 (m, 1H), 2.79–3.00 (m, 4H), 1.84 (q, *J* = 8.0 Hz, 2H), 1.34 (t, *J* = 7.4 Hz, 3H), 1.08 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 162.6, 145.0, 136.4, 132.7, 131.9, 131.7, 130.3, 128.9, 128.5, 119.2, 114.2, 37.7, 25.2, 22.6, 14.3, 14.2 ppm; IR (KBr): $\bar{\nu}$ = 2,963, 1,594, 1,477, 1,377, 1,345, 1,184, 911 cm^{-1}; MS (EI): *m/z* = 279 $[M + 1]^+$; HRMS (EI): 278.0539 $[M + H]^+$.

2-(Dec-9-enyl)-6-methoxy-3-(non-8-enyl)quinoline
(**3j**, $C_{29}H_{43}NO$)
Yield 86%; colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 9.0 Hz, 1H), 7.77 (s, 1H), 7.26 (d, *J* = 9.0 Hz, 1H), 7.01 (s, 1H), 6.80 (d, *J* = 9.2 Hz, 1H), 6.61 (d, *J* = 8.8 Hz, 1H), 5.76–5.91 (m, 3H), 4.93–5.06 (m, 6H), 3.93 (s, 3H), 2.95 (t, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H), 2.06 (m, 4H), 1.19–1.78 (m, 17H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 162.6, 139.9, 139.7, 135.4, 134.7, 129.3, 128.8, 127.6, 127.2, 126.3, 117.6, 114.6, 114.3, 113.2, 59.3, 50.3, 44.6, 36.4, 34.3, 32.5, 30.7, 30.6, 30.5, 30.2, 30.0, 29.9, 29.8, 29.6, 29.3, 29.2, 29.1, 27.6 ppm; IR (KBr): $\bar{\nu}$ = 3,074, 2,925, 1,624, 1,513, 1,493, 1,381, 1,229, 1,165, 1,034, 909 cm^{-1}; MS (EI): *m/z* = 421 $[M]^+$; HRMS (EI): 422.3417 $[M + H]^+$.

2-(Dec-9-enyl)-3-(non-8-enyl)quinoline (**3k**, $C_{28}H_{41}N$)
Yield 86%; colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.0 Hz, 1H), 7.86 (s, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.64 (dd, *J* = 7.2 Hz, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 7.2 Hz, *J* = 8.2 Hz, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 5.73–5.94 (m, 3H), 4.93–5.06 (m, 6H), 2.99 (t, *J* = 8.0 Hz, 2H), 2.80 (d, *J* = 8.0 Hz, 2H), 2.07 (m, 4H),1.34–1.58 (m, 18H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 162.7, 139.7, 139.5, 135.3, 134.5, 129.6, 128.8, 128.7, 127.3, 126.0, 117.5, 114.6, 114.5, 113.1, 50.2, 44.4, 36.3, 34.2, 32.8, 30.9, 30.3, 30.2, 30.1, 30.0, 29.9, 29.8, 29.7, 29.5, 29.4, 29.3, 27.6 ppm; IR (KBr): $\bar{\nu}$ = 2,925, 1,640, 1,603, 1,505, 1,491, 1,319, 992, 909 cm^{-1}; MS (EI): *m/z* = 391 $[M]^+$; HRMS (EI): 392.3316 $[M + H]^+$.

6-Bromo-2-(dec-9-enyl)-3-(non-8-enyl)quinoline
(**3l**, $C_{28}H_{40}BrN$)
Yield 83%; colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.0 Hz, 1H), 7.71–7.76 (m, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.50 (d, *J* = 8.8 Hz, 2H), 5.73–5.90 (m, 3H), 4.93–5.06 (m, 6H), 3.07 (t, *J* = 7.2 Hz, 2H), 2.96 (t, *J* = 8.0 Hz, 1H), 2.82 (t, *J* = 6.8 Hz, 1H), 2.06 (m, 4H), 1.33–1.65 (m, 17H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.6, 140.3, 139.6, 135.3, 134.5, 130.2, 128.8, 128.2, 127.6, 127.3, 126.0, 119.8, 117.5, 114.6, 50.2, 44.4, 36.3, 34.2, 32.8, 30.9, 30.3, 30.2, 30.2, 30.0, 29.9, 29.8, 29.7, 29.5, 29.4, 29.3, 27.6 ppm; IR (KBr): $\bar{\nu}$ = 2,925, 1,640, 1,596, 1,497, 1,317, 1,260, 1,177, 1,072, 995, 909 cm^{-1}; MS (EI): *m/z* = 472 $[M + 2]^+$; HRMS (EI): 470.2418 $[M + 1]^+$.

3-Benzyl-6,7-dimethyl-2-(2-phenylethyl)quinoline
(**4a**, $C_{26}H_{25}N$)
Yield 83%; white solid; m.p.: 97–100 °C; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.89 (s, 1H), 7.67 (s, 1H), 7.48 (s, 1H), 7.11–7.36 (m, 10H), 4.07 (s, 2H), 3.17–3.26 (m, 2H), 3.08 (t, *J* = 5.2 Hz, 2H), 2.50 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 160.2, 146.0, 142.1, 139.6, 139.0, 135.7, 135.5, 131.5, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.0, 126.4, 126.3, 126.0, 125.8, 38.7, 37.7, 35.5, 20.4, 20.0 ppm; IR (KBr): $\bar{\nu}$ = 3,025, 2,916, 1,602, 1,493, 1,453, 1,074, 1,028 cm^{-1}; MS (EI): *m/z* = 351 $[M]^+$; HRMS (EI): 352.2062 $[M + H]^+$.

2-Benzyl-6,7-dimethyl-3-phenylquinoline (**4b**, $C_{24}H_{21}N$)
Yield 78%; light yellow oil; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.86 (s, 1H), 7.55 (s, 1H), 7.41–7.11 (m, 8H), 6.98–6.94 (m, 2H), 4.33 (s, 2H), 2.52 (s, 3H), 2.48 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.4, 146.8,

140.4, 140.1, 140.0, 136.6, 136.3, 135.7, 129.9, 129.2, 128.7, 128.6, 128.4, 127.8, 127.0, 126.2, 43.1, 20.9, 20.5 ppm; IR (KBr): $\bar{\nu} = 3{,}037$, 2,912, 1,601, 1,478, 1,453, 1,074, 948 cm^{-1}; MS (EI): $m/z = 323$ $[M]^+$; HRMS (EI): 324.1746 $[M + H]^+$.

2-Benzyl-3-(2-phenylethyl)benzo[f]quinoline (**5a**, $C_{28}H_{23}N$)
Yield 70%; light yellow oil; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 9.57$ (d, $J = 7.6$ Hz, 1H), 8.01 (d, $J = 7.4$ Hz, 1H), 7.78–8.00 (m, 4H), 7.21–7.56 (m, 11H), 4.20 (s, 2H), 3.36–3.42 (m, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 157.8$, 140.4, 140.3, 137.2, 136.6, 134.1, 131.9, 130.0, 129.7, 129.6, 129.3, 129.1, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.4, 126.4, 125.5, 125.1, 124.8, 43.2, 41.2, 39.4 ppm; MS (EI): $m/z = 373$ $[M]^+$; HRMS (EI): 374.1908 $[M + H]^+$.

3-Benzyl-2-phenylbenzo[f]quinoline (**5b**, $C_{26}H_{19}N$)
Yield 70%; light yellow oil; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 9.48$ (d, $J = 8.0$ Hz, 1H), 7.95–8.03 (m, 2H), 7.68–7.86 (m, 4H), 7.24–7.51 (m, 10H), 4.49 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 157.9$, 140.2, 140.1, 137.2, 136.6, 134.1, 131.7, 130.3, 129.6, 129.6, 129.3, 129.1, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.4, 126.4, 125.6, 125.3, 125.0, 43.0 ppm; MS (EI): $m/z = 345$ $[M]^+$; HRMS (EI): 346.15 $[M + H]^+$.

Acknowledgments The authors thank "the Fundamental Research Funds for the Central Universities" (JUSRP10905), the "Start-up grant of Jiangnan University" (1045210372090460) for financial support.

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