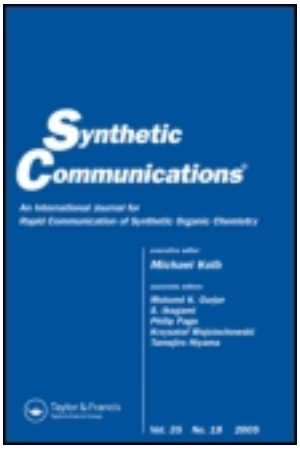

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Version of record first published: 12 Aug 2009

To cite this article: Xiao-Liang Zhang, Qiu-Ying Wang, Shou-Ri Sheng, Qing Wang & Xiao-Ling Liu (2009): Efficient Friedländer Synthesis of Quinoline Derivatives from 2-Aminoarylketones and Carbonyl Compounds Mediated by Recyclable PEG-Supported Sulfonic Acid, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 39:18, 3293-3304

To link to this article: http://dx.doi.org/10.1080/00397910902754283

Synthetic Communications®, 39: 3293–3304, 2009

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910902754283

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Efficient Friedländer Synthesis of Quinoline Derivatives from 2-Aminoarylketones and Carbonyl Compounds Mediated by Recyclable PEG-Supported Sulfonic Acid

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Abstract: 2-Aminoarylketones undergo smooth condensation with α-methylene ketones in the presence of 10 mol% of poly(ethylene glycol) (PEG)–supported sulfonic acid under mild reaction conditions to afford the corresponding poly-substituted quinolines in excellent yields. The catalyst can be recovered by simple filtration and can be recycled in subsequent reactions. The method is simple, cost-effective, and environmentally benign.

Keywords: 2-Aminoarylketone, α-methyleneketone, PEG-supported sulfonic acid, quinoline

Quinolines and their derivatives are very important compounds because of their wide occurrence in natural products[1] and their interesting biological activities as antimalarial, anti-inflammatory, antiasthmatic, antibacterial, antihypertensive, and tyrosine kinase–inhibiting agents.[2] Additionally, quinolines are valuable synthons used for the preparation of nanostructures and polymers that combine enhanced electronic, optoelectronic, or nonlinear optical properties with excellent mechanical properties.[3] Various methods such as Skraup, Doebner–von Miller, Friedländer, and

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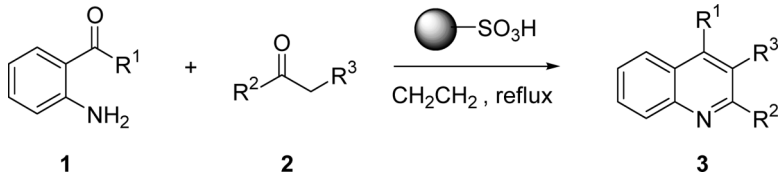
Combes reactions have been developed for the preparation of quinolines,[4–6] Among these methods, Friedländer annulation,[6a] an acid- or base-catalyzed condensation followed by a cycoldehydration between an aromatic 2-aminoaldehyde or ketone and a carbonyl compound containing a reactive α-methylene group, is one of the simplest and most straightforward protocols for the synthesis of poly-substituted quinolines. Brønsted acid catalysts, such as NH_2SO_3H, HCl, H_2SO_4, *p*-toluenesulfonic acid (*p*-TSA), H_3PO_4, trifluoroacetic acid (TFA), $NaHSO_4 \cdot SiO_2$, and $HClO_4 \cdot SiO_2$, were widely used[7] for Friedländer annulation. However, many of these methods require high temperature (150–200 °C) and extended reaction times, which lead to several side reactions. Under thermal and basic conditions, 2-aminobezophenone fails to react with cyclohexanone, deoxybenzoin, and β-ketoesters.[8] Recently, Lewis acids such as $FeCl_3$, $Mg(ClO_4)_2$, $CuSO_4 \cdot 5H_2O$, $FeSO_4 \cdot 7H_2O$, $SnCl_2$, $AlCl_3$, $Bi(OTf)_3$, $Sc(OTf)_3$, $Y(OTf)_3$, $CeCl_3 \cdot 7H_2O$, I_2, NaF, TMSCl, $NaAuCl_4 \cdot 2H_2O$, $Nd(NO_3)_3 \cdot 6H_2O$, and $Ag_3POW_{12}O_{40}$ have been found to be effective for this conversion.[9] Additionally, ionic liquid[10] and microwave irradiation[11] have been employed to promote the Friedländer reaction. Even some of these methods also suffer form harsh reaction conditions, poor yields, high temperature, tedious workup, and the use of stoichiometric and relatively expensive reagents. Thus, the development of simple, convenient, and environmentally friendly approaches for the synthesis of quinolines is still in demand. Over the past few years, there has been a considerable growth in interest in the use of soluble polymer-supported catalysts and reagents in organic synthesis because of their low cost, ease of preparation, simple workup, and recoverablity of catalysts.[12] As part of an ongoing research program focused on the use poly(ethylene glycol) (PEG)–bound sulfonic acid in organic synthesis,[13] we examined the synthesis of poly-substituted quinolines using PEG-bound sulfonic acid as an efficient and recyclable catalyst through condensation/annulation reaction of 2-aminoarylketones and carbonyl compounds. Herein, we report the results of this study (Scheme 1).

As we recently reported, PEG-supported sulfonic acid with a loading of 0.22 mmol/g was prepared readily from the dihydroxy PEG 4000 in



Scheme 1. Friedländer synthesis of quinolines catalyzed by PEG-bound sulfonic acid.

three steps.[13] To optimize the reaction conditions, we first conducted the Friedländer condensation of 2-aminoacetophenone with ethyl acetoacetate (**2a**) to the desired ethyl 2,4-dimethylquinoline-3-carboxylate (**3a**) using a catalytic amount of PEG-supported sulfonic acid at room temperature in different solvents such as CH_3OH, Et_2O, CH_3CN, and CH_2Cl_2. To our delight, after a series of experiments, the best results were obtained when the reaction was carried out in CH_2Cl_2 at reflux room temperature for 40 min in the presence of 10 mol% of PEG-supported sulfonic acid with respect to 2-aminoacetophenone (Table 1, entry 1). Furthermore, it was found that the use of 10 mol% of the catalyst was sufficient to promote the reaction, and greater amounts of the catalyst did not improve the yields. However, in the absence of PEG-supported sulfonic acid, the reaction did not proceed even after long reaction times (12–24 h). Furthermore, the condensation of 2-aminoacetophenone with **2a** in the presence of concd. H_2SO_4 afforded **3a** in only 68% yield (Table 1, entry 2). A possible mechanism for the synthesis of quinolines using this method is shown in Scheme 2, based on the literature[9a] and the obtained results.

To study the generality of this process, several examples were studied. As seen from Table 1, 2-aminoacetophenone could be replaced by 2-aminobezophenone, and α-methylene ketones could be extended from ethyl acetoacetate (**2a**) to methyl acetoacetate (**2b**), acyclic 1,3-diketones

Table 1. PEG-bound sulfonic acid–catalyzed Friedländer synthesis of quinolines **3**

Entry	R^1	R^2	R^3	Time (min)	Product	Yield (%)[a]
1	CH_3	CH_3	CO_2Et	40	**3a**	96
2	CH_3	CH_3	CO_2Et	90	**3a**	68[b]
3	CH_3	CH_3	CO_2Me	40	**3b**	95
4	CH_3	CH_3	COMe	50	**3c**	92
5	CH_3	$CH_2CH_2CH_2CO$		75	**3d**	94
6	CH_3	$CH_2C(CH_3)_2CH_2CO$		90	**3e**	96
7	CH_3	$CH_2(CH_2)_2CH_2$		60	**3f**	90
8	CH_3	$CH_2CH_2CH_2$		55	**3g**	90
9	C_6H_5	CH_3	CO_2Et	40	**3h**	94
10	C_6H_5	CH_3	CO_2Me	40	**3i**	94
11	C_6H_5	CH_3	COMe	45	**3j**	94
12	C_6H_5	$CH_2CH_2CH_2CO$		80	**3k**	92
13	C_6H_5	$CH_2C(CH_3)_2CH_2CO$		90	**3l**	95
14	C_6H_5	$CH_2(CH_2)_2CH_2$		65	**3m**	92
15	C_6H_5	$CH_2CH_2CH_2$		50	**3n**	92

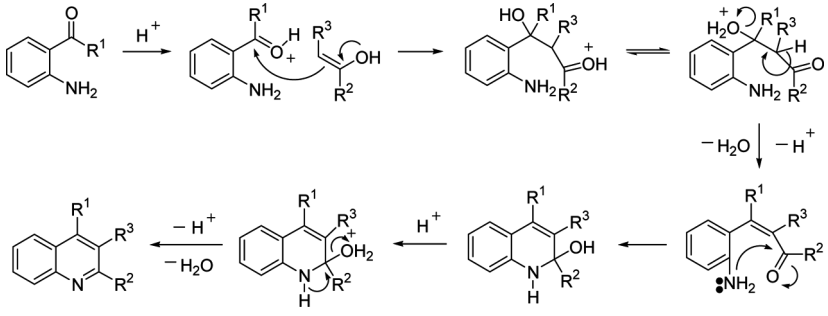
[a]Yields refer to pure isolated products.
[b]Concd. H_2SO_4 used instead of PEG-bound sulfonic acid.

such as 2,4-pentanedione (**2c**), cyclic 1,3-diketones such as 1,3-cyclohexanedione (**2d**) and 5,5-dimethyl-1,3-cyclohexanedione (**2e**), and simple cyclic ketones such as cyclohexanone (**2f**) and cyclopentanone (**2g**). In the optimized reaction conditions, a library synthesis of quinoline **3a–n** was successfully obtained in very good yields (90–96%) by Friedländer condensation between 2-aminoacetophenone as well as 2-aminobezophenone with a variety of carbonyl compounds **2a–g** in the presence of PEG-supported sulfonic acid.

After finishing the condensation reaction, dichloromethane (DCM) was evaporated, and the PEG-bound sulfonic acid was readily recovered by precipitation with cold diethyl ether, followed by filtration and washing with diethyl ether (average recovery yields ranged from 92 to 95%) for the next run directly without any activation. The recovered PEG-bound sulfonic acid was reused consecutively without losing any significant activity. For example, the reaction of 2-aminoacetophenone and **2a** afforded the corresponding quinoline **3a** in 95%, 92%, 90%, and 88% yields over four runs. It should be noted that when the catalytic activity of polymeric sulfonic acid decreased, the resin could be treated with concd. HCl again to keep its catalytic activity.[13] Furthermore, this method is clean and free from side reactions.

On the other hand, the efficacy of the PEG-bound sulfonic acid as a catalyst for the synthesis of **3a** as a model compound was compared with that of several reported catalysts such as sulfamic acid, $NaHSO_4$–SiO_2, $Y(OTf)_3$, and ionic liquid (Table 2). It indicated that PEG-bound sulfonic acid is a very efficient catalyst useful in the synthesis of quinoline derivatives. From the practical point of view, the catalyst is inexpensive, nontoxic, and readily available, and the reaction proceeded in shorter times. Furthermore, the catalyst can be easily recovered and reused.

In summary, we have described a mild, efficient, and environmentally benign protocol for the synthesis of quinolines and polycyclic quinolines



Scheme 2. A possible mechanism for the synthesis of quinolines.

Table 2. Comparison of the efficiency of PEG-bound sulfonic acid for synthesis of **3a**

Entry	Catalyst	Time (min)	Yield (%)[a]	Ref.
1	NH_2SO_3H	90	89	7c
2	$NaHSO_4$–SiO_2	240	80	7e
3	$Y(OTf)_3$	360	83	9i
4	Ionic liquid	180	94	10b

[a]Yields refer to pure isolated products.

via Friedländer condensation of 2-aminoarylketones with α-methylene ketones using PEG-bound sulfonic acid as a recyclable catalyst. This method offers good advantages such as short reaction times, good yields, readily available recovery, and reuse of the catalyst combined with the straightforward and easy workup procedure.

EXPERIMENTAL

Melting points were uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker Avance (400-MHz) spectrometer, using $CDCl_3$ as the solvent and tetramethylsilane (TMS) as internal standard. Fourier transform–infrared (FT-IR) spectra were taken on a Perkin-Elmer SP One FT-IR spectrophotometer. Microanalyses were performed with a Carlo Erba 1106 elemental analyzer. PEG-bound sulfonic acid was prepared according to our report method.[13] The other reagents were purchased from commercial sources and were used without further purification.

General Procedure for the Preparation of Quinoline Derivatives (3a–n)

PEG-bound sulfonic acid (0.1 mmol, 0.45 g) was added to a solution of 2-aminoarylketone (1.0 mmol) and α-methyleneketone (1.2 mmol) in DCM (10.0 mL), and the reaction mixture was stirred at reflux temperature for the appropriate time according to Table 1. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the organic solvent was removed in vacuum, and the mixture was cooled to room temperature. Then cold diethyl ether (100 mL) was added with vigorous stirring. For completion of the precipitation, the suspension was left at 0°C for another 30 min. The recovered PEG-bound sulfonic acid was then collected by filtration and washed with cold diethyl

ether (2×20 mL) for the next run. The filtrated organic solution was concentrated to afford crude product, which was purified by silica-gel column chromatography (10% ethyl acetate in hexane) to afford a pure product. All the products were characterized by ^{1}H NMR, ^{13}C NMR, FT-IR, and microanalysis and also by comparison with authentic samples.

Data

Ethyl 2,4-Dimethylquinoline-3-carboxylate (**3a**)

Oil (lit.[10b] oil); ^{1}H NMR: $\delta = 7.98$ (d, $J = 8.4$ Hz, 1 H), 7.90 (d, $J = 8.4$ Hz, 1 H), 7.66 (t, $J = 7.6$ Hz, 1 H), 7.45 (t, $J = 7.6$ Hz, 1 H), 4.46 (q, $J = 7.1$ Hz, 2 H), 2.70 (s, 3 H), 2.61 (s, 3 H), 1.40 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR: $\delta = 168.8$, 154.1, 147.2, 141.2, 129.6, 129.4, 127.7, 126.1, 125.6, 123.7, 61.1, 23.5, 15.6, 14.0; IR (neat): $\nu = 3070$, 2930, 2872, 1725, 1615, 1590, 1214, 1081, 578 cm^{-1}. Anal. calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.22; H, 6.67; N, 6.02.

Methyl 2,4-Dimethylquinoline-3-carboxylate (**3b**)

Oil (lit.[9c] oil); ^{1}H NMR: $\delta = 8.04$ (d, $J = 8.4$ Hz, 1 H), 7.95 (d, $J = 8.3$ Hz, 1 H), 7.65 (t, $J = 7.5$ Hz, 1 H), 7.45 (t, $J = 7.5$ Hz, 1 H), 3.60 (s, 3 H), 2.71 (s, 3 H), 2.64 (s, 3 H). ^{13}C NMR: $\delta = 168.5$, 154.4, 147.0, 141.3, 129.6, 128.8, 127.7, 126.2, 125.8, 123.6, 52.5, 23.9, 15.8; IR (neat): $\nu = 3067$, 2953, 1730, 1613, 1585, 1485, 1445, 1423, 1390, 1230, 1170, 1065, 965, 762, 700 cm^{-1}. Anal. calcd. for $C_{13}H_{13}NO_2$: C, 72.52; H, 6.09; N, 6.51. Found: C, 72.62; H, 6.18; N, 6.59.

1-(2,4-Dimethylquinolin-3-yl)ethanone (**3c**)

Oil (lit.[10b] oil); ^{1}H NMR: $\delta = 7.99$ (d, $J = 8.4$ Hz, 1 H), 7.91 (d, $J = 8.4$ Hz, 1 H), 7.66 (t, $J = 7.6$ Hz, 1 H), 7.49 (t, $J = 7.6$ Hz, 1 H), 2.61 (s, 3 H), 2.58 (s, 3 H), 2.56 (s, 3 H); IR (neat): $\nu = 3067$, 2958, 1703, 1614, 1585, 1208, 758 cm^{-1}; ^{13}C NMR: $\delta = 206.2$, 152.5, 146.6, 138.4, 135.5 (2 C), 129.6, 129.0, 126.2, 123.4, 32.5, 23.2, 15.0. Anal. calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.27; H, 6.50; N, 7.11.

9-Methyl-3,4-Dihydroacridin-1(2*H*)-one (**3d**)

Solid; mp 66–67°C (lit.[7d] mp 65–66 °C); ^{1}H NMR: $\delta = 8.08$ (d, $J = 8.0$ Hz, 1 H), 7.94 (d, $J = 8.0$ Hz, 1 H), 7.59–7.50 (m, 2 H), 3.12–3.10 (m, 2 H),

2.80–2.77 (m, 2 H), 2.61–2.58 (m, 2 H), 2.21 (s, 3 H), 1.85–1.82 (m, 2 H); ^{13}C NMR: δ = 199.5, 160.1, 149.2, 147.6, 130.9, 120.0, 127.2, 126.5, 125.1, 124.3, 40.3, 34.0, 20.6, 15.6; IR (KBr): ν = 3030, 2928, 1570, 1478, 1348, 1165, 1076, 938, 820, 775, 708, 618 cm^{-1}. Anal. calcd. for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.70; H, 6.28; N, 6.71.

3,3,9-Trimethyl-3,4-dihydroacridin-1(2*H*)-one (**3e**)

Solid; mp 107–108°C (lit.[7d] mp 105–106 °C); ^{1}H NMR: δ = 8.20 (d, *J* = 8.4 Hz, 1 H), 8.01 (d, *J* = 8.4 Hz, 1 H), 7.76 (t, *J* = 7.5 Hz, 1 H), 7.56 (t, *J* = 7.5 Hz, 1 H), 3.20 (s, 2 H), 3.07 (s, 3 H), 2.65 (s, 2 H), 1.14 (s, 6 H); ^{13}C NMR: δ = 200.2, 160.9, 149.5, 148.1, 131.2, 120.1, 127.5, 126.3, 125.4, 124.1, 54.7, 48.3, 31.9, 28.2 (2 C), 15.8; IR (KBr): ν = 2956, 2968, 1684, 1560, 1495, 1375, 1280, 1214, 764 cm^{-1}. Anal. calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.22; H, 7.24; N, 5.78.

9-Methyl-1,2,3,4-tetrahydroacridine (**3f**)

Solid; mp 76–78°C (lit.[10b] mp 78 °C); ^{1}H NMR: δ = 7.82–7.24 (m, 4 H), 2.95 (t, *J* = 7.6 Hz, 2 H), 2.60 (t, *J* = 7.6 Hz, 2 H), 2.26 (s, 3 H), 1.74–1.72 (m, 4 H); ^{13}C NMR: δ = 157.8, 145.5, 140.6, 128.5, 127.6, 126.4 (2 C), 124.6, 122.8, 33.8, 26.5, 22.8, 22.3, 12.9; IR (KBr): ν = 3066, 2936, 1615, 1580, 1351, 754 cm^{-1}. Anal. calcd. for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10. Found: C, 85.13; H, 7.76; N, 7.03.

9-Methyl-2,3-dihydro-1*H*-cyclopenta[b]quinoline (**3g**)

Solid; mp 59–61°C (lit.[10b] mp 60 °C); ^{1}H NMR: δ = 8.00–7.45 (m, 4 H), 3.31 (t, *J* = 7.0 Hz, 2 H), 2.98 (t, *J* = 7.5 Hz, 2 H), 2.50 (s, 3 H), 2.22–2.20 (m, 2 H); ^{13}C NMR: δ = 166.7, 147.1, 137.7, 133.6, 128.8, 127.8, 126.9, 125.0, 123.1, 34.7, 29.5, 22.6, 14.6; IR (KBr): ν = 3065, 2956, 1614, 908, 751 cm^{-1}. Anal. calcd. for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64. Found: C, 85.12; H, 7.06; N, 7.73.

Ethyl 2-Methyl-4-phenylquinoline-3-carboxylate (**3h**)

Solid; mp 97–98°C (lit.[9n] mp 99 °C); ^{1}H NMR: δ = 8.06 (d, *J* = 8.4 Hz, 1 H), 7.70 (t, *J* = 7.9 Hz, 1 H), 7.56–7.35 (m, 7 H), 4.09 (q, *J* = 7.1 Hz, 2 H), 2.80 (s, 3 H); 0.96 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR: δ = 167.8, 153.5, 147.8, 145.6, 135.7 (2C), 129.5, 129.0, 128.2, 127.8, 126.5, 126.1, 125.0,

96.1, 68.9, 23.3, 13.5; IR (KBr): $\nu = 3060$, 2975, 1725, 1604, 1580, 1486, 1443, 1230, 1068, 904, 700 cm^{-1}. Anal. calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.42; H, 5.96; N, 4.88.

Methyl 2-Methyl-4-phenylquinoline-3-carboxylate (**3i**)

Solid; mp 87–88°C (lit.[9n] mp 86–88 °C); ^{1}H NMR: $\delta = 8.10$ (d, $J = 8.4$ Hz, 1 H), 8.07–7.35 (m, 8 H), 3.58 (s, 3 H), 2.79 (s, 3 H); ^{13}C NMR: $\delta = 169.0$, 154.5, 147.8, 146.4, 135.7, 130.3, 129.2, 128.9, 128.5, 128.3, 127.3, 126.5, 125.1, 52.2, 23.9; IR (KBr): $\nu = 3065$, 2952, 1732, 1613, 1584, 1426, 1395, 1231, 1171, 1068, 764, 702 cm^{-1}. Anal. calcd. for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.05; H, 5.56; N, 5.12.

1-(2-Methyl-4-phenylquinolin-3-yl)ethanone (**3j**)

Solid; mp 105–106°C (lit.[9e] mp 105–106 °C); ^{1}H NMR: $\delta = 8.02$ (d, $J = 8.0$ Hz, 1 H), 7.75–7.35 (m, 8 H), 2.68 (s, 3 H), 1.98 (s, 3 H); ^{13}C NMR: $\delta = 205.5$, 153.0 (2C), 146.9, 144.3, 134.6 (2C), 129.4 (2C), 128.5, 128.1, 125.0, 125.5, 124.5, 31.5, 23.4; IR (KBr): $\nu = 3028$, 2960, 1705, 1610, 1568, 1486, 1396, 1215, 768, 705 cm^{-1}. Anal. calcd. for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.65; H, 5.87; N, 5.43.

9-Phenyl-3,4-dihydroacridin-1(2*H*)-one (**3k**)

Solid; mp 139–140°C (lit.[9c] mp 140–142 °C); ^{1}H NMR: $\delta = 8.04$ (d, $J = 8.7$ Hz, 1 H), 7.45–7.40 (m, 6 H), 7.20–7.17 (m, 2 H), 3.35 (t, $J = 6.5$ Hz, Hz, 2 H), 2.68 (t, $J = 6.5$ Hz, 2 H), 2.28–2.25 (m, 2 H); ^{13}C NMR: $\delta = 197.1$, 161.7, 150.7, 148.2, 137.2, 131.1, 128.7, 128.5, 128.1, 127.8, 127.0, 125.9, 125.2, 123.4, 40.1, 34.2, 20.9; IR (KBr): $\nu = 3032$, 2946, 1690, 1553, 1485, 1390, 1220, 1160, 1023, 770, 706, 540 cm^{-1}. Anal. calcd. for $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.12. Found: C, 83.60; H, 5.64; N, 5.03.

3,3-Dimethyl-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**3l**)

Solid; mp 190–191°C (lit.[9c] mp 190–192 °C); ^{1}H NMR: $\delta = 8.04$ (d, $J = 8.0$ Hz, 1 H), 7.74 (t, $J = 7.8$ Hz, 1 H), 7.48–7.35 (m, 5 H), 7.20–7.12 (m, 2 H), 3.30 (s, 2 H), 2.56 (s, 2 H), 1.20 (s, 6 H); ^{13}C NMR: $\delta = 198.3$, 161.4, 149.9, 148.2, 137.5, 131.3, 128.8, 128.6, 128.2, 127.5, 126.8, 125.6, 125.1, 124.0, 54.3, 48.2, 31.6, 28.0 (2 C), 15.6; IR (KBr): $\nu = 3060$, 2956,

1712, 1602, 1574, 1208, 1380, 740 cm^{-1}. Anal. calcd. for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.75; H, 6.27; N, 4.73.

9-Phenyl-1,2,3,4-tetrahydroacridine (**3m**)

Yellow solid; mp 131–132°C (lit.[9c] mp 132 °C); ^1H NMR: $\delta = 8.00$ (d, $J = 8.1$ Hz, 1 H), 7.62–7.42 (m, 5 H), 7.30–7.19 (m, 3 H), 3.20 (t, $J = 6.8$ Hz, Hz, 2 H), 2.60 (t, $J = 6.6$ Hz, 2 H), 2.04–1.96 (m, 2 H), 1.84–1.74 (m, 2 H); ^{13}C NMR: $\delta = 158.5$, 146.5, 146.0, 137.5, 129.3, 128.8, 128.6, 128.2, 127.8, 127.5, 126.7, 125.5, 125.2, 34.2, 27.9, 23.2, 22.6; IR (KBr): $\nu = 3060$, 2940, 1610, 1575, 1486, 1440, 1220, 768, 710 cm^{-1}. Anal. calcd. for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found: C, 88.06; H, 6.68; N, 5.52.

9-Phenyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline (**3n**)

Yellow solid; mp 114–115°C (lit.[9c] mp 113–115 °C); ^1H NMR: $\delta = 8.00$–7.45 (m, 4 H), 3.31 (t, $J = 7.0$ Hz, 2 H), 2.98 (t, $J = 7.5$ Hz, 2 H), 2.50 (s, 3 H), 2.22–2.20 (m, 2 H); ^{13}C NMR: $\delta = 166.7$, 147.1, 137.7, 133.6, 128.8, 127.8, 126.9, 125.0, 123.1, 34.7, 29.5, 22.6, 14.6; IR (KBr): $\nu = 3065$, 2956, 1614, 1569, 1478, 1348, 1165, 1076, 940, 820, 775, 708 cm^{-1}. Anal. calcd. for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.24; H, 6.26; N, 5.78.

ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the National Natural Science Foundation (NSF) of China (No. 20562005), NSF of Jiangxi Province (Nos. 0620021 and 2007GZW0185), and the Research Program of Jiangxi Province Department of Education (No. GJJ08165).

REFERENCES

1. (a) Morimoto, Y.; Matsuda, F.; Shirahama, H. Total synthesis of (±)-virantmycin and determination of its stereochemistry. *Synlett* **1991**, 202–203; (b) Balasubramanian, M.; Keay, J. G. In *Comprehensive Heterocyclic Chemistry II*; A. R. Katritzky, C. W. Rees, E. F. V. Scriven (Eds.); Pergamon: New York, 1996; vol. 5, p 245; (c) Michael, J. P. Quinoline, quinazoline, and acridone alkaloids. *Nat. Prod. Rep.* **1997**, *14*, 605–618.
2. (a) Maguire, M. P.; Sheets, K. R.; McVety, K.; Spada, A. P.; Zilberstein, A. A new series of PDGF receptor tyrosine kinase inhibitors: 3-Substituted

quinoline derivatives. *J. Med. Chem.* **1994**, *37*, 2129–2133; (b) Roma, G.; Braccio, M. D.; Grossi, G.; Mattioli, F.; Ghia, M. 1,8-Naphthyridines, IV: 9-Substituted *N,N*-dialkyl-5-(alkylamino or cycloalkylamino) [1,2,4] triazolo[4,3-*a*][1,8]naphthyridine-6-carboxamides, new compounds with anti-aggressive and potent anti-inflammatory activities. *Eur. J. Med. Chem.* **2000**, *35*, 1021–1035; (c) Chen, Y.-L.; Fang, K.-C.; Sheu, J.-Y.; Hsu, S.-L.; Tzeng, C.-C. Synthesis and antibacterial evaluation of certain quinolone derivatives. *J. Med. Chem.* **2001**, *44*, 2374–2376.

3. (a) Agrawal, A. K.; Jenekhe, S. A. Electrochemical properties and electronic structures of conjugated polyquinolines and polyanthrazolines. *Chem. Mater.* **1996**, *8*, 579–589; (b) Jenekhe, S. A.; Lu, L.; Alam, M. M. M. New conjugated polymers with donor–acceptor architectures: Synthesis and photophysics of carbazole-quinoline and phenothiazine-quinoline copolymers and oligomers exhibiting large intramolecular charge transfer. *Macromolecules* **2001**, *34*, 7315–7324; (c) Jégou, G.; Jenekhe, S. A. Highly fluorescent poly(arylene ethynylene)s containing quinoline and 3-alkylthiophene. *Macromolecules* **2001**, *34*, 7926–7928.
4. (a) Abass, M. Fused quinolines: Recent synthetic approaches to azoloquinolines: A review. *Heterocycles* **2005**, *65*, 901–965; (b) Kouznetsov, V. V.; Mendez, L. Y. V.; Gomez, C. M. M. Recent progress in the synthesis of quinolines. *Curr. Org. Chem.* **2005**, *9*, 141–143.
5. (a) Jiang, B.; Si, Y.-G. Zn(II)-mediated alkynylation-cyclization of *o*-trifluoroacetyl anilines: One-pot synthesis of 4-trifluoromethyl-substituted quinoline derivatives. *J. Org. Chem.* **2002**, *67*, 9449–9451; (b) Cho, C. S.; Oh, B. H.; Kim, J. S.; Kim, T.-J.; Shim, S. C. Synthesis of quinolines *via* rutheniumcatalysed amine exchange reaction between anilines and trialkylamines. *Chem. Commun.* **2000**, 1885–1886 (and references therein).
6. (a) Cheng, C.-C.; Yan, S.-J. The Friedländer synthesis of quinolines. *Org. React.* **1982**, *28*, 37–39; (b) Linderman, R. J.; Kirolloss, K. S. Regioselective synthesis of trifluoromethyl substituted quinolines from trifluoroacetyl acetylenes. *Tetrahedron Lett.* **1990**, *31*, 2689–2692; (c) Arisawa, M.; Theeraladanon, C.; Nishinda, A.; Nakagawa, M. Synthesis of substituted 1,2-dihydroquinolines and quinolines using ene–ene metathesis and ene–enol ether metathesis. *Tetrahedron Lett.* **2001**, *42*, 8029–8033; (d) Theoclitou, M. E.; Robinson, L. A. Novel facile synthesis of 2,2,4-substituted 1,2-dihydroquinolines via a modified Skraup reaction. *Tetrahedron Lett.* **2002**, *43*, 3907–3910; (e) Dumouchel, S.; Mongin, F.; Trecourt, F.; Queguiner, G. Tributylmagnesiumate complex-mediated bromine–magnesium exchange of bromoquinolines: A convenient access to functionalized quinolines. *Tetrahedron Lett.* **2003**, *44*, 2033–2035; (f) Denmark, S. E.; Venkatraman, S. On the mechanism of the Skraup–Doebner–Von Miller quinoline synthesis. *J. Org. Chem.* **2006**, *71*, 1668–1676.
7. (a) Strekowski, L.; Czamy, A. The Friedländer synthesis of 4-perfluoroalkylquinolines. *J. Fluor. Chem.* **2000**, *104*, 281–284; (b) Hu, Y.-Z.; Zang, G.; Thummel, R. P. Friedländer approach for the incorporation of 6-bromoquinoline into novel chelating ligands. *Org. Lett.* **2003**, *5*, 2251–2253; (c) Yadav,

J. S.; Rao, P. P.; Sreenu, D.; Rao, R. S.; Kumar, V. N.; Nagaiah, K.; Prasad, A. R. Sulfamic acid: An efficient, cost-effective, and recyclable solid acid catalyst for the Friedländer quinoline synthesis. *Tetrahedron Lett.* **2005**, *46*, 7249–7253; (d) Wang, G.-W.; Jia, C.-S.; Dong, Y.-W. Benign and highly efficient synthesis of quinolines from 2-aminoarylketone or 2-aminoarylaldehyde and carbonyl compounds mediated by hydrochloric acid in water. *Tetrahedron Lett.* **2006**, *47*, 1059–1063; (e) Desai, U. V.; Mitragotri, S. D.; Thopate, T. S.; Pore, D. M.; Wadgaonkar, P. P. A highly efficient synthesis of trisubstituted quinolines using sodium hydrogensulfate on silica gel as a reusable catalyst. *Arkivoc* **2006**, 198–204; (f) Narasimhulu, M.; Reddy, T. S.; Mahesh, K. C.; Prabhakar, P.; Rao, C. B.; Venkateswarlu, Y. Silica supported perchloric acid: A mild and highly efficient heterogeneous catalyst for the synthesis of poly-substituted quinolines via Friedländer hetero-annulation. *J. Mol. Catal. A: Chem.* **2007**, *266*, 114–117.

8. Fehnel, E. A. Friedlander syntheses with *o*-aminoaryl ketones, III: Acid-catalyzed condensations of *o*-aminobenzophenone with polyfunctional carbonyl compounds. *J. Heterocycl. Chem.* **1967**, *4*, 565–570.
9. (a) Arcadi, A.; Chiarini, M.; Di Giuseppe, S.; Marinelli, F. A new green approach to the Friedländer synthesis of quinolines. *Synlett* **2003**, 203–206, and references therein; (b) McNaughton, B. R.; Miller, B. L. A mild and efficient one-step synthesis of quinolines. *Org. Lett.* **2003**, *5*, 4257–4259; (c) Yadav, J. S.; Reddy, B. V. S.; Premlatha, P. $Bi(OTf)_3$-catalyzed Friedländer hetero-annulation: A rapid synthesis of 2,3,4-trisubstituted quinolines. *Synlett* **2004**, 963–966; (d) Yadav, J. S.; Reddy, B. V. S.; Premlatha, P.; Rao, R. S.; Nagaiah, K. Silver phosphotungstate: A novel and recyclable heteropoly acid for Friedländer quinoline synthesis. *Synthesis* **2004**, 2381–2385; (e) Bose, D. S.; Kumar, R. K. An efficient, high-yielding protocol for the synthesis of functionalized quinolines via the tandem addition/annulation reaction of o-aminoaryl ketones with α-methylene ketones. *Tetrahedron Lett.* **2006**, *47*, 813–816; (f) Mogilaih, K.; Reddy, C. S. An efficient Friedländer condensation using sodium fluoride as catalyst in the solid state. *Synth. Commun.* **2003**, 3131–3134; (g) Wu, J.; Xia, H.-G.; Gao, K. An international journal for the quickest publication of high-quality research covering the breadth of synthetic, physical and biomolecular organic chemistry. *Org. Biomol. Chem.* **2006**, *4*, 126–129; (h) Walser, A.; Flyll, T.; Fryer, R. T. Nucleophilic displacement of aromatic fluorine, part IV. Quinolinoquinolines and benzochromenoquinolines. *J. Heterocycl. Chem.* **1975**, *12*, 737–741; (i) De, S. K.; Gibbs, R. A. A mild and efficient one-step synthesis of quinolines. *Tetrahedron Lett.* **2005**, *46*, 1647–1649; (j) Arumugam, P.; Karthikeyan, G.; Atchudan, R.; Muralidharan, D.; Perumal, P. T. A simple, efficient and solvent-free protocol for the Friedländer synthesis of quinolines by using $SnCl_2 \cdot 2H_2O$. *Chem. Lett.* **2005**, *34*, 314–315; (k) Wu, J.; Zhang, L.; Diao, T.-N. An expeditious approach to quinolines via Friedländer synthesis catalyzed by $FeCl_3$ or $Mg(ClO_4)_2$. *Synlett* **2005**, 2653–2657; (l) De S, K.; Gibbs, R. A. A mild and efficient one-step synthesis of quinolines. *Tetrahedron Lett.* **2005**, *46*, 1647–1649; (m) Varala, R.; Enugala, R.; Adapa, S. R. Efficient and

rapid Friedländer synthesis of functionalized quinolines catalyzed by neodymium(III) nitrate hexahydrate. *Synthesis* **2006**, 3825–3830; (n) Zolfigol, M. A.; Salehi, P.; Ghaderia, A.; Shiria, M. Iodine-catalyzed Friedländer quinoline synthesis under solvent-free conditions. *J. Chin. Chem. Soc.* **2007**, *54*, 267–271; (o) Ryabukhin, S. V.; Volochnyuk, D. M.; Plaskon, A. S.; Naumchik, V. S.; Tolmachev, A. A. Chlorotrimethylsilane-mediated Friedländer synthesis of polysubstituted quinolines. *Synthesis* **2007**, 1214–1224.

10. (a) Wang, J.; Fan, X.; Zhang, X.; Han Can, L. Green preparation of quinoline derivatives through $FeCl_3 \cdot 6H_2O$-catalyzed Friedländer reaction in ionic liquids. *Can. J. Chem.* **2004**, *82*, 1192–1196. (b) Palimkar, S. S.; Siddiqui, S. A.; Daniel, T.; Lahoti, R. J.; Srinivasan, J. V. Ionic liquid–promoted regiospecific Friedländer annulation: Novel synthesis of quinolines and fused polycyclic quinolines. *J. Org. Chem.* **2003**, *68*, 9371–9376; (c) Karthikeyan, G.; Perumal, P. T. A mild, efficient, and improved protocol for the Friedländer synthesis of quinolines using Lewis acidic ionic liquid. *J. Heterocycl. Chem.* **2004**, *41*, 1039–1042.
11. (a) Song, S. J.; Cho, S. J.; Park, D. K.; Kwon, T. W.; Jenekhe, S. A. Microwave-enhanced solvent-free synthesis of a library of quinoline derivatives. *Tetrahedron Lett.* **2003**, *44*, 255–257; (b) Muscia, G. C.; Bollini, M.; Carnevale, J. P.; Bruno, A. M.; Asís, S. E. Microwave-assisted Friedländer synthesis of quinolines derivatives as potential antiparasitic agents. *Tetrahedron Lett.* **2006**, *47*, 8811–8815.
12. (a) Dickerson, T. J.; Reed, N. N.; Janda, K. D. Soluble polymers as scaffolds for recoverable catalysts and reagents. *Chem. Rev.* **2002**, *102*, 3325–3344; (b) Benaglia, M.; Puglisi, A.; Cozzi, F. Polymer-supported organic catalysts. *Chem. Rev.* **2003**, *103*, 3401–3430.
13. Wang, Q.-Y.; Sheng, S.-R.; Wei, M.-H.; Xie, Z.-L.; Liu, X.-L. PEG-supported sulfonic acid as an efficient and recyclable catalyst for the synthesis of 1,1-diacetates under solvent-free conditions. *Synth. Commun.* **2007**, *37*, 1019–1026.