A HIGHLY EFFECTIVE ONE-POT SYNTHESIS OF QUINOLINES FROM 2-ALKYNYLNITROBENZENES

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Abstract – A highly effective one-pot synthesis of poly-substituted quinolines from 2-alkynylnitrobenzenes using inexpensive reagents has been developed. Reaction of 2-alkynylnitrobenzenes with Sn/HCl in EtOH resulted in the formation of 2-aminophenyl ketones and subsequently condensed in situ with ketones to form tri-substituted quinolines in 80-97% yields.

INTRODUCTION

Palladium-catalyzed cross-coupling reactions between terminal alkynes and aryl halides, known as the Sonogashira reaction, have been used extensively in natural products chemistry and materials science for the synthesis of substituted and conjugated alkynes. 1 If 2-alkynylnitrobenzenes (1) prepared from Sonogashira coupling reaction were reduced and hydrated in one-pot operation, the corresponding vinyl alcohols were easily rearranged to 2-aminophenyl ketones (2), which are useful intermediates for many heterocycles such as quinolines, imidazoles, benzotriazoles, and benzodiazepines. 2 Especially, quinolines and their derivatives are very important compounds because of their wide occurrence in natural products and biologically active compounds. 3 Amongst various methodologies reported for the preparation of quinolines, Friedländer annulation is one of the simplest and most straightforward protocols. 4 One of the drawbacks of this method remains the relative instability of the intermediate 2-aminobenzaldehydes or 2-aminophenyl ketones, which can readily undergo self-condensation. These results prompted us to investigate the one-pot synthesis of quinolines from 2-alkynylnitrobenzenes by reduction, hydration and acidic cyclization by Friedländer reaction. We report herein the one-pot synthesis of 2,3,4-trisubstituted quinolines from 2-alkynylnitrobenzenes.

RESULTS AND DISCUSSION

2-Alkynylnitrobenzenes were synthesized from 2-iodonitrobenzene and terminal alkynes by Sonogashira coupling reaction. 1 We first tried the reduction and hydration of 2-phenylethynylnitrobenzene (1a) (Scheme 1). Treatment of 1a with Sn (1 eq) and Na2S (0.3 eq) followed by the addition of conc. HCl (4
eq) resulted in the formation of 1-(2-aminophenyl)-2-phenylethanone (2a) in 50% yield (entry 1, Table 1). When conc. HCl (10 eq) was added to a suspension of 1a and Sn (2 eq) and Na2S (0.3 eq) in refluxing EtOH for 8 h, 2a was obtained in 90% yield, indicating that reduction and hydration were performed in one-pot operation (entry 2). 0.3 eq of Na2S is essential for the present reaction, because, in the absence of Na2S, less than 10% of 2-phenylindole was obtained as a side product, suggesting that a very small amount of palladium chloride catalyzed the intramolecular cyclization (entry 3). When Zn or Fe was used as a reducing reagent, 2a was also obtained in 50% and 65% yields, respectively (entries 4 and 5). Thus, Sn found to be a better reducing reagent for the synthesis of 2-aminophenyl ketones. Other substituted 2-alkynylnitrobenzenes 1b-i gave 2-aminophenyl ketones 2b-i in good yields (entries 6-13).

![Scheme 1](image)

**Table 1. Reaction of 2-Alkynylnitrobenzene 1 with Sn, Zn, or Fe/HCl**

<table>
<thead>
<tr>
<th>Entry</th>
<th>1</th>
<th>Metal (eq)</th>
<th>HCl /eq</th>
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<th>Yield /%</th>
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<tr>
<td>1</td>
<td>1a</td>
<td>Sn (1)</td>
<td>4</td>
<td>2a</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>Sn (2)</td>
<td>10</td>
<td>2a</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>Sn (2)</td>
<td>10</td>
<td>2a</td>
<td>65a</td>
</tr>
<tr>
<td>4</td>
<td>1a</td>
<td>Zn (3)</td>
<td>10</td>
<td>2a</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>1a</td>
<td>Fe (3)</td>
<td>10</td>
<td>2a</td>
<td>65</td>
</tr>
<tr>
<td>6</td>
<td>1b</td>
<td>Sn (2)</td>
<td>10</td>
<td>2b</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>1c</td>
<td>Sn (2)</td>
<td>10</td>
<td>2c</td>
<td>98</td>
</tr>
<tr>
<td>8</td>
<td>1d</td>
<td>Sn (2)</td>
<td>10</td>
<td>2d</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td>1e</td>
<td>Sn (2)</td>
<td>10</td>
<td>2e</td>
<td>74</td>
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<tr>
<td>10</td>
<td>1f</td>
<td>Sn (2)</td>
<td>10</td>
<td>2f</td>
<td>93</td>
</tr>
<tr>
<td>11</td>
<td>1g</td>
<td>Sn (2)</td>
<td>10</td>
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<td>73</td>
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<tr>
<td>12</td>
<td>1h</td>
<td>Sn (2)</td>
<td>10</td>
<td>2h</td>
<td>75</td>
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<tr>
<td>13</td>
<td>1i</td>
<td>Sn (2)</td>
<td>10</td>
<td>2i</td>
<td>84</td>
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</table>

a) The reaction was carried out in the absence of Na2S (8% of 2-phenylindole was obtained as a side product).

Simple 2-aminophenylethanones, such as 2-aminoacetophenone and 2-aminobenzophenone, were commercially available; however, few reports on the synthesis of more complicated 2-aminophenyl
ketones 2 were known. Among them are photo Fries rearrangement, reduction of 2-nitrophenyl ketones, o-acylation of anilines, and addition of 2-cyanoanilines with Grignard reagents. The present method provides a general method on the synthesis of 2.

We then investigated tandem synthesis of quinolines from 2-alkynylnitrobenzenes, Sn/HCl, and acetylacetone by a combination of reduction/hydration and Friedländer reaction. Acidic Friedlander reaction was generally carried out acetic acid as a solvent. If we want to synthesize quinolines in one-pot operation, other solvent should be required. Thus, we first tried the reaction of 2a with acetylacetone and sulfuric acid in acetic acid gave 2-methyl-3-acetyl-4-phenylquinoline (3a) in 96% yield. When the reaction was carried out by using HCl as acid in refluxing ethanol, 3a was obtained in 91% yield (Scheme 2).

Scheme 2

Then one-pot reaction was carried out under these conditions (conc HCl in refluxing EtOH).

Treatment of 1a with Sn (2 eq)/HCl (10 eq), Na2S (0.3 eq), and acetylacetone (1.2 eq) in refluxing EtOH for 18 h gave 2-methyl-3-acetyl-4-benzylquinoline (3a) in 89% yield (entry 1, Table 2). As shown in Table 2, quinolines 3b-i were obtained in 80-93% yields (Scheme 3). Thus, one-pot synthesis of quinolines from 2-alkynylnitrobenzenes was accomplished.

Scheme 3
Table 2. One-pot synthesis of quinolines from 1

<table>
<thead>
<tr>
<th></th>
<th>Time / h</th>
<th>Product</th>
<th>Yield / %</th>
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<tbody>
<tr>
<td>1a</td>
<td>18</td>
<td>3a</td>
<td>89</td>
</tr>
<tr>
<td>1b</td>
<td>18</td>
<td>3b</td>
<td>80</td>
</tr>
<tr>
<td>1c</td>
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<td>86</td>
</tr>
<tr>
<td>1d</td>
<td>18</td>
<td>3d</td>
<td>87</td>
</tr>
<tr>
<td>1e</td>
<td>20</td>
<td>3e</td>
<td>95</td>
</tr>
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<td>1f</td>
<td>21</td>
<td>3f</td>
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</tr>
<tr>
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<td>27</td>
<td>3g</td>
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</tr>
<tr>
<td>1h</td>
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<td>76</td>
</tr>
<tr>
<td>1i</td>
<td>27</td>
<td>3i</td>
<td>67</td>
</tr>
</tbody>
</table>

Similarly, one-pot synthesis of quinolines from cyclohexanone was accomplished (Scheme 4).

![Scheme 4](image)

While 2-alkynylnitrobenzenes were easily synthesized by the CuI-PdCl$_2$ catalyzed reaction of 2-iodonitrobenzene with terminal alkynes, we finally tried the one-pot synthesis of 2,3,4-trisubstituted quinolines from 2-iodonitrobenzene. Treatment of 2-iodonitrobenzene with ethynylbenzene in the presence of catalytic amount of PdCl$_2$-CuI in refluxing Et$_2$N, followed by the evaporation and addition of Sn/HCl and acetylacetone in refluxing ethanol resulted in the formation of 3a in 65% yield (Scheme 5).

![Scheme 5](image)

In summary, we have accomplished the general synthesis of 2-aminophenyl ketones from 2-alkynylnitrobenzenes. One-pot reaction of 2-alkynylnitrobenzenes with ketones afforded the corresponding quinolines in high yields. Thus, general and convenient synthesis of polysubstituted quinolines from 2-nitroalkynylnitrobenzenes was achieved.

**EXPERIMENTAL**

**General**
All chemicals were obtained from commercial suppliers and were used without further purification. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254) and flash column chromatography was performed with silica (Merck, 70-230 mesh). NMR spectra (1H at 400 MHz; 13C at 100 MHz) were recorded in CDCl3, and chemical shifts are expressed in ppm relative to internal TMS for 1H- and 13C-NMR. Melting points were uncorrected.

Materials: 2-Alkynylnitrobenzenes were synthesized by Sonogashira coupling reaction.1 1-Butyl-4-(2-(nitrophenyl)ethyl)benzene 1d: red needles. mp 146-148 0C 1H NMR (CDCl3) δ = 0.92 (t, 3H, J = 7.4 Hz, CH3), 1.33 (dt, 2H, J = 7.4 and 7.4 Hz, CH2), 1.57-1.60 (m, 2H, CH2), 2.61 (dd, 2H, J = 7.6 and 7.8 Hz, CH2), 7.18 (dd, 2H, J = 8.0 Hz, Ar), 7.42 (dd, 1H, J = 7.6 and 7.8 Hz, Ar), 7.50 (d, 2H, J = 8.0 Hz, Ar), 7.56 (dd, 1H, J = 7.6 and 8.0 Hz, Ar), 7.69 (d, 1H, J = 7.8 Hz, Ar), 8.06 (d, 1H, J = 8.0 Hz, Ar). 13C NMR (CDCl3) δ = 14.15 (CH3), 22.54 (CH2), 33.58 (CH2), 35.92 (CH2), 84.92 (Me), 97.84 (C), 119.75, 124.93, 128.51, 128.83, 132.19, 132.21, 132.99, 134.74, 144.83 (Ar). HRMS: Calcd for C13H17NO2: 279.1259. Found: (M+) 279.1258.

Synthesis of 1-(2-aminophenyl)-2-phenylethanone 2a
To a suspension of 2-phenylethynynitrobenzene 1a (0.11 g, 0.50 mmol), Sn (0.12 g, 1.0 mmol) and Na2S H2O (0.036 g, 0.15 mmol) in EtOH:H2O (9:1, 5 mL) was added conc. HCl (0.42 mL, 5.0 mmol) in one portion. After refluxing for 8 h, the reaction mixture was washed with 5% aq. Na2CO3 (10 mL) and extracted with EtOAc (10 mL x 3). The combined extracts were dried over magnesium sulfate, filtered, and evaporated to give yellow crystals, which was chromatographed over silica gel by elution with hexane:EtOAc (5:1) to give yellow leaflets of 1-(2-aminophenyl)-2-phenylethanone 2a (0.095 g, 0.41 mmol) was obtained in 82%. Compound 2a: mp 99-100 0C (lit.2 mp 98-99 0C). 1H NMR (CDCl3) δ = 4.26 (s, 2H, CH2), 6.29 (br, 2H, NH), 6.63-6.66 (m, 2H, Ar), 7.23-7.26 (m, 4H, Ar), 7.31 (dd, 2H, J = 7.4 Hz and 8.0 Hz, Ar), 7.82 (d, 1H, J = 8.4 Hz, Ar). 13C NMR (CDCl3) δ = 46.33 (CH2), 116.04, 117.66, 117.74, 126.98, 128.83, 129.72, 131.81, 134.71, 135.62, 151.07 (Ar), 200.20 (CO).

Other 2-aminophenylethanones were obtained in a similar manner.

1-(2-Aminophenyl)-1-hexan-1-one 2b (0.19 g, 0.93 mmol, 93%). Yellow oil.8 1H NMR (CDCl3) δ = 0.90 (dd, 3H, J = 6.0 Hz and 6.4 Hz, CH3), 1.35-1.38 (m, 4H, CH2), 1.70 (dt, 2H, J = 7.2 Hz and 7.4 Hz, CH2), 2.91 (t, 2H, J = 7.5 Hz, CH2), 6.25 (br, 2H, NH2), 6.62-6.66 (m, 2H, Ar), 7.23-7.27 (m, 1H, Ar), 7.73 (d, 1H, J = 8.0 Hz, Ar). 13C NMR (CDCl3) δ = 14.21 (Me), 22.80, 24.92, 31.88, 39.51 (CH2), 115.94, 117.58, 118.26, 131.45, 134.33, 150.58 (Ar), 203.44 (C=O).

1-(2-Aminophenyl)-1-heptan-1-one 2c (0.11 g, 0.49 mmol, 98%). Yellow oil.9 1H NMR (CDCl3) δ = 0.88 (dd, 3H, J = 6.8 Hz and 7.0 Hz, Me), 1.30-1.40 (m, 6H, CH2), 1.68 (dt, 2H, J = 7.6 Hz and 7.6 Hz, CH2), 2.91 (t, 2H, J = 7.5 Hz, CH2), 6.26 (br 2H, NH2), 6.67-6.70 (m, 2H, Ar), 7.24-7.28 (m, 1H, Ar), 7.74 (d, 1H, J = 8.0 Hz, Ar). 13C NMR (CDCl3) δ = 14.27 (Me), 22.27, 25.18, 29.36, 31.93, 39.55 (CH2), 115.92, 117.56, 118.26, 131.44, 134.30, 150.56 (Ar), 203.41 (C=O).

1-(2-Aminophenyl)-2-(4-butylphenylethanone 2d (0.16 g, 0.60 mmol, 86%). Colorless leaflets: mp 72-73 0C. 1H-NMR (CDCl3) δ = 0.90 (dd, 3H, J = 7.4 Hz and 7.4 Hz, Me), 1.32 (dt, 2H, J = 7.4 Hz and 7.6 Hz, CH2), 1.57-1.60 (m, 2H, CH2), 1.57-1.60 (m, 2H, CH2), 2.56 (dd, 2H, J = 7.6 Hz and 7.8 Hz, CH2), 4.22 (s, 2H, CH2), 6.23 (br, 2H, NH2), 6.63-6.66 (m, 2H, Ar), 7.13 (d, 2H, J = 8.4 Hz, Ar), 7.16 (d, 2H, J = 8.4 Hz, Ar), 7.25-7.27 (m, 1H, Ar), 7.84 (d, 1H, J = 8.2 Hz, Ar). 13C NMR (CDCl3) δ = 14.21 (Me), 22.65, 33.82, 35.53, 45.94, (CH2), 116.01, 117.64, 117.81, 128.90, 129.55, 131.86, 132.70, 130.64, 141.56, 151.09 (Ar), 200.46 (C=O). Anal. Calcd for C18H21NO: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.86; H, 7.78; N, 5.27.

1-(2-Aminophenyl)-4-hydroxy-1-butanol-1-one 2e (0.066 g, 0.37 mmol, 74%). Pale brown oil.10 1H NMR (CDCl3) δ = 1.99 (dt, 2H, J = 6.0 Hz and 6.8 Hz, CH2), 3.09 (t, 2H, J = 6.8 Hz, CH2), 3.73 (t, 2H, J = 6.0 Hz), 6.66-6.68 (m, 2H, Ar), 7.26-7.27 (m, 1H, Ar), 7.76 (d, 1H, J = 8.0 Hz, Ar). 13C NMR (CDCl3) δ = 27.67, 36.16, 62.60 (CH2), 116.06, 117.64, 118.03, 131.45, 134.64, 150.65 (Ar), 203.14 (C=O). HRMS: Calcd for C19H13NO2: 179.0946. Found: (M+) 179.0942.

1-(2-Aminophenyl)-3,3-dimethyl-1-butanol-1-one 2f 0.18 g, 0.93 mmol, 93%). Yellow oil. 1H NMR (CDCl3) δ = 1.06 (s, 9H, 3Me), 2.82 (s, 2H, CH2), 6.29 (br, 2H, NH2), 6.58-6.62 (m, 2H, Ar), 7.19-7.23
One-pot Synthesis of Quinoline 6a from 1a

To a solution of 2a with acetylacetone (acidic Friedländer reaction) 6.65 (s, 1H, Ar), 7.23-7.35 (m, 5H, Ar), 7.74 (d, 1H, Ar), 8.03 (d, 1H, J = 8.8 Hz, Ar). 13C NMR (CDCl3) δ = 30.50 (Me), 31.96 (C(Me)3), 50.77 (CH2), 115.75, 117.57, 119.73, 132.24, 134.25, 150.59 (Ar), 203.40 (C=O). HRMS: Calcd for C12H12NO; 191.1310. Found: (M+) 191.1315.

1-(2-Amino-4-chlorophenyl)-2-phenyletanone 2g (0.090 g, 0.37 mmol, 73%). Yellow leaflets: mp 98-99 °C. 1H NMR (CDCl3) δ = 4.22 (s, 2H, CH2), 6.37 (br, 2H, NH2), 6.59 (d, 1H, J = 8.8 Hz, Ar), 6.65 (1H, Ar), 7.23-7.35 (m, 5H, Ar), 7.74 (d, 1H, J = 8.8 Hz, Ar). 13C NMR (CDCl3) δ = 46.43 (CH2), 116.19, 116.49, 116.80, 127.13, 128.91, 129.63, 133.18, 135.29, 141.62, 151.90, (Ar), 199.50 (C=O). HRMS: Calc for C12H12ClNO; 225.0612.

2a (0.072 mL, 0.72 mmol) in 10 mL of EtOH:H2O (9:1) was added to this solution. The mixture was extracted with EtOAc (5 mL x 3). Other reactions were carried out in a similar manner by using 0.3 mmol of 3.

One-pot Synthesis of Quinoline 6a from 1a

To a solution of 3a (0.125 g, 0.45 mmol). Colorless amorphous solid. mp 84-86 °C. 1H NMR (CDCl3) δ = 2.26 (s, 3H, Me), 4.26 (s, 2H, CH2), 6.13 (br, 2H, NH2), 6.58 (d, 1H, J = 8.0 Hz, Ar), 7.09 (d, 1H, J = 8.0 Hz, Ar), 7.26-7.36 (m, 5H, Ar), 7.64 (1H, Ar). 13C NMR (CDCl3) δ = 20.75 (Me), 46.21 (CH), 55.47 (OMe), 99.55, 104.91, 112.33, 126.91, 128.84, 129.68, 130.00, 136.13, 153.74, 164.44 (Ar), 198.53 (C=O). HRMS: Calc for C15H15NO3; 241.1103. Found; (M+) 241.1100.

3a: colorless amorphous solid. mp 84-86 °C. 1H NMR (CDCl3) δ = 2.42 (s, 3H, Me), 2.68 (s, 3H, Me), 4.37 (s, 2H, CH2), 7.06 (d, 2H, J = 6.3 Hz, Ar), 7.16-7.24 (m, 3H, Ar), 7.44 (dd, 1H, J = 7.7 Hz and 8.4 Hz, Ar), 7.66 (dd, 1H, J = 7.7 Hz and 8.4 Hz, Ar), 7.87 (d, 1H, J = 8.4 Hz, Ar), 8.03 (d, 1H, J = 8.4 Hz, Ar). 13C NMR (CDCl3) δ = 23.92, 32.85 (Me), 34.92 (CH2), 124.87, 125.83, 126.87, 126.88, 128.49, 129.98, 129.62, 130.15, 136.77, 138.62, 140.59, 147.85, 153.15 (Ar), 206.77 (CO). HRMS: Calc for C19H17NO5; 375.1310. Found; (M+) 375.1303.

3-Acetyl-2-methyl-4-pentylquinoline 3b (0.061 g, 0.24 mmol, 80%). Yellow oil. 1H NMR (CDCl3) δ = 0.90 (dd, 3H, J = 7.2 Hz and 7.6 Hz, Me), 1.34-1.46 (m, 4H, CH2), 1.64-1.70 (m, 2H, CH2), 2.60 (s, 3H, Me), 2.63 (s, 3H, Me), 2.87 (t, 2H, J = 8.4 Hz, CH2), 7.52 (dd, 1H, J = 7.6 Hz and 8.4 Hz, Ar), 7.67 (dd, 1H, J = 7.6 Hz and 8.4 Hz, Ar), 7.96 (d, 1H, J = 8.4 Hz, Ar). HRMS: Calc for C17H17NO; 255.1623. Found: (M+) 255.1623.

3-Acetyl-4-hexyl-2-methylquinoline 3c (0.069 g, 0.26 mmol, 86%). Yellow oil. 1H NMR (CDCl3) δ = 0.90 (dd, 3H, J = 6.6 Hz and 7.0 Hz, Me), 1.30-1.34 (m, 4H, CH2), 1.44-1.48 (m, 2H, CH2), 1.62-1.69 (m, 2H, CH2), 2.59 (s, 3H, Me), 2.63 (s, 3H, Me), 2.86 (t, 2H, J = 8.2 Hz, CH2), 7.52 (dd, 1H, J = 7.6 Hz and 8.4 Hz, Ar), 7.67 (dd, 1H, J = 7.6 Hz and 8.4 Hz, Ar), 7.96 (d, 1H, J = 8.4 Hz, Ar), 8.02 (d, 1H, J =
9-Hexyl-5,6,7,8-tetrahydroacridine

\[ \text{206.97} (\text{C=O}). \quad \text{HRMS: Calcd for C}_{43}\text{H}_{34}\text{N} + \]

3-Acetyl-(4-butylbenzyl)-2-methylquinoline

\[ \text{Ar}). \quad \text{88-89 (CDCl}_3 \text{).} \quad \text{Found; (M}^+ \text{)} 269.1737. \]

3-Acetyl-(4-hydroxypropyl)-2-methylquinoline

\[ \text{3d (0.074 g, 0.29 mmol, 95%). Pale brown oil.} \quad \text{1H NMR (CDCl}_3 \text{)} \delta = 1.65 \text{ (br, 1H, OH), 1.93-1.99 (m, 2H, CH}_2 \text{), 2.62 (s, 3H, Me), 2.65 (s, 3H, Me), 3.05 (dd, 2H, J = 7.4 Hz and 7.6 Hz, CH}_2 \text{), 3.67 (dd, 2H, J = 5.6 Hz and 5.6 Hz, CH}_2 \text{), 7.54 (dd, 1H, J = 7.2 and 7.6 Hz, Ar), 7.70 (dd, 1H, J = 7.2 Hz and 7.6 Hz, Ar), 7.98 (d, 1H, J = 8.4 Hz, Ar), 8.02-8.05 (d, 1H, J = 8.4 Hz and 8.4 Hz, Ar), 8.78 (d, 1H, J = 8.4 Hz, Ar), 8.02 (d, 1H, J = 8.4 Hz, Ar).} \quad \text{13C NMR (CDCl}_3 \text{)} \delta = 23.84 (Me), 26.29, 33.06 (CH}_2 \text{), 33.90 (Me), 61.78 (CH}_2 \text{), 124.16, 125.28, 126.73, 129.67, 130.08, 135.82, 143.05, 147.68, 152.78 (Ar), 207.62 (CO). \quad \text{HRMS: Calcd for C}_{124}\text{H}_{172}\text{N}_2O_2; 331.1936.} \quad \text{Found; (M}^+ \text{)} 331.1937. \]

3-Acetyl-2-methyl-4-neopentylquinoline

\[ \text{3e (0.069 g, 0.29 mmol, 95%). Yellow granules: mp 88-89 °C.} \quad \text{1H NMR (CDCl}_3 \text{)} \delta = 2.42 (s, 3H, Me), 2.67 (s, 3H, Me), 4.33 (s, 2H, CH}_2 \text{), 7.04 (d, 2H, J = 7.4 Hz, Ar), 7.20-7.26 (m, 3H, Ar), 7.37 (d, 1H, J = 8.8 Hz, Ar), 7.78 (d, 1H, J = 8.8 Hz, Ar), 8.03 (s, 1H, Ar).} \quad \text{13C NMR (CDCl}_3 \text{)} \delta = 23.92, 32.78 (Me), 34.96 (CH}_2 \text{), 124.29, 126.28, 127.02, 127.80, 128.40, 128.60, 129.08, 135.95, 136.88, 138.28, 140.73, 148.34, 154.56 (C=O), 206.29 (CO).} \quad \text{HRMS: Calcd for C}_{19}\text{H}_{16}^{35}\text{CINO; 309.0920.} \quad \text{Found; (M}^+ \text{)} 309.0925. \]

3-Acetyl-4-benzyl-7-chloro-2-methylquinoline

\[ \text{3g (0.056 g, 0.18 mmol, 60%). Yellow granules: mp 88-89 °C.} \quad \text{1H NMR (CDCl}_3 \text{)} \delta = 2.39 (s, 3H, Me), 2.65 (s, 3H, Me), 3.94 (s, 3H, OMe), 4.33 (s, 2H, CH}_2 \text{), 7.05 (d, 2H, J = 7.2 Hz, Ar), 7.08 (d, 1H, J = 9.2 Hz, Ar), 7.18-7.25 (m, 3H, Ar), 7.37 (s, 1H, Ar), 7.75 (d, 1H, J = 9.2 Hz, Ar).} \quad \text{13C NMR (CDCl}_3 \text{)} \delta = 22.60, 31.67 (Me), 33.62 (CH}_2 \text{), 55.49 (OMe), 106.34, 118.59, 119.59, 124.76, 125.55, 127.20, 127.69, 133.61, 137.47, 139.50, 148.49, 152.23, 159.87 (Ar), 205.65 (C=O).} \quad \text{HRMS: Calcd for C}_{20}\text{H}_{15}\text{N}_2O_2; 305.1416.} \quad \text{Found; (M}^+ \text{)} 305.1408. \]

3-Acetyl-4-benzyl-2-methylquinoline

\[ \text{3i (0.058 g 0.20 mmol) in 67% yield. Yellow granules: mp 123-124 °C.} \quad \text{1H NMR (CDCl}_3 \text{)} \delta = 2.37 (s, 3H, Me), 2.44 (s, 3H, Me), 2.65 (s, 3H, Me), 4.34 (s, 2H, CH}_2 \text{), 7.06 (d, 2H, J = 7.2 Hz, Ar), 7.18-7.26 (m, 3H, Ar), 7.49 (d, 1H, J = 8.4 Hz, Ar), 7.64 (s, 1H, Ar),} \quad \text{13C NMR (CDCl}_3 \text{)} \delta = 22.13, 23.75, 32.78 (Me), 34.70 (CH}_2 \text{), 123.68, 123.70, 125.83, 126.80, 128.49, 128.95, 129.29, 132.28, 136.73, 138.72, 139.90, 146.42, 152.00 (Ar), 206.97 (C=O).} \quad \text{HRMS: Calcd for C}_{20}\text{H}_{15}\text{N}_2O_2; 289.1467.} \quad \text{Found; (M}^+ \text{)} 289.1467. \]

9-Hexyl-5,6,7,8-tetrahydroacridine

\[ \text{3j (0.055 g, 0.20 mmol) in 68%). Yellow oil.} \quad \text{1H NMR (CDCl}_3 \text{)} \delta = 0.90 (dd, 3H, J = 6.8 Hz and 6.8 Hz, Me), 1.32-1.48 (m, 4H, CH}_2 \text{), 1.48 (dt, 2H, J = 6.8 Hz and 7.0 Hz, CH}_2 \text{), 1.56 (dt, 2H, J = 6.8 Hz and 8.0 Hz, CH}_2 \text{), 1.93-1.98 (m, 4H, CH}_2 \text{), 2.92 (dd, 2H, J = 7.6 Hz and 8.0 Hz, CH}_2 \text{), 3.11 (dd, 2H, J = 6.0 Hz and 6.2 Hz, CH}_2 \text{), 3.74 (dd, 1H, J = 7.6 Hz and 8.0 Hz, Ar), 7.57 (dd, 1H, J = 7.6 Hz and 8.4 Hz, Ar), 7.93 (d, 1H, J = 8.0 Hz, Ar), 7.96 (d, 1H, J = 8.4 Hz, Ar).} \quad \text{13C NMR (CDCl}_3 \text{)} \delta = 14.33 (Me), 22.90, 23.04, 23.46, 26.57, 27.90, 29.84, 30.24, 31.91, 34.74 (CH}_2 \text{), 123.54, 125.47, 126.41, 128.22, 128.25, 129.33, 145.94, 146.55, 159.04 (Ar).} \quad \text{HRMS: Calcd for C}_{19}\text{H}_{25}\text{N}; 267.1978.} \quad \text{Found; (M}^+ \text{)} 267.1989. \]
9-Neopentyl-5,6,7,8-tetrahydroacridine 3k (0.043 g, 0.17 mmol, 57%). Yellow oil. $^1$H NMR (CDCl$_3$) δ = 0.98 (s, 9H, Me), 1.86-1.97 (m, 4H, CH$_2$), 2.94 (dd, 2H, $J = 6.0$ Hz and 6.2 Hz, CH$_2$), 3.09-3.16 (m, 4H, CH$_2$), 7.39 (dd, 1H, $J = 7.2$ Hz and 8.0 Hz, Ar), 7.55 (dd, 1H, $J = 7.2$ Hz and 8.0 Hz, Ar), 7.95 (d, 1H, $J = 8.0$ Hz, Ar), 8.02 (d, 1H, $J = 8.0$ Hz, Ar). $^{13}$C NMR (CDCl$_3$) δ = 22.67, 23.16, 28.09 (CH$_2$), 31.22 (Me), 34.42, 34.82 (CH$_2$), 38.71 (C(Me)$_2$). 124.70, 125.49, 127.98, 128.02, 130.92, 143.22, 146.51, 159.27 (Ar). HRMS: Calcd for C$_{18}$H$_{23}$N: 253.1830. Found; (M$^+$) 253.1826.

**One-pot synthesis of quinoline 3a from 2-iodonitrobenzene.**

To a suspension of 2-iodonitrobenzene (0.124 g, 0.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (0.004 g, 0.005 mmol), and CuI (0.005 g, 0.025 mmol) in diethylamine (8 mL) was added phenylacetylene (0.066 mL, 0.6 mmol). After refluxing for 6 h, the suspension was evaporated and added Sn (0.118 gm 1.0 mmol), CuI (0.005 g, 0.025 mmol) in diethylamine (8 mL) was added phenylacetylene (0.066 mL, 0.6 mmol) in one portion. After refluxing for 16 h, the suspension was evaporated and added Sn (0.118 gm 1.0 mmol), Na$_2$S·9H$_2$O (0.060 g, 0.25 mmol), acetylacetone (0.062 mL, 0.6 mmol), EtOH (6 mL), H$_2$O (1 mL), and HCl (0.42 mL, 5 mmol). After refluxing for 16 h, 5% aq. Na$_2$CO$_3$ was added and extracted with EtOAc (5mL x 3). The combined extract was dried over magnesium sulfate, filtered, and evaporated to give brown solid, which was chromatographed over silica gel by elution with hexane: EtOAc (5:1) to afford quinoline 3a (0.088 g, 0.33 mmol, 65%). Other reactions were carried out in a similar manner.

**REFERENCES**


