Efficient and Rapid Friedlander Synthesis of Functionalized Quinolines Catalyzed by Neodymium(III) Nitrate Hexahydrate

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Received 26 June 2006; revised 13 July 2006

Abstract: Friedlander synthesis of quinolines catalyzed by neodymium nitrate [$Nd(NO_3)_3·6H_2O$, 5 mol%] in ethanol at room temperature was achieved in moderate to excellent yields (62–94%).

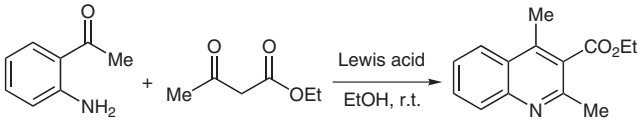
Key words: 2-aminophenyl ketones, neodymium(III) nitrate, quinolines, annulations, domino reactions

Quinolines are important scaffolds with wide applications in medicinal chemistry,[1] as antimalarial, anti-inflammatory, antiasthmatic, antibacterial, antihypertensive, and tyrosine kinase PDGF-RTK inhibiting agents.[2] In addition, quinolines are valuable synthons, used for assembling nano- and mesostructures with enhanced electronic and photonic properties.[3] Although other methods such as Skraup, Doebner von Miller, and Combes procedures have been reported[4] for the preparation of quinolines, the Friedlander annulation is one of the most simple and straightforward methods for the synthesis of substituted quinolines.

The Friedlander synthesis is an acid- or base-catalyzed condensation between a 2-aminoaryl ketone and a second carbonyl compound containing a reactive α-methylene group followed by a cyclodehydration. Generally, this reaction is carried out by refluxing an aqueous or alcoholic solution of reactants in the presence of base at high temperature.[5] Under thermal- or base-catalysis conditions, 2-aminophenyl phenyl ketone fails to react with simple ketones such as cyclohexanone and β-keto esters.[6] Recently, Lewis acids such as $ZnCl_2$, NaF, $FeCl_3$, $Sc(OTf)_3$, silver phosphotungstate, ionic liquids, $NaAuCl_4·2H_2O$, and molecular iodine have been shown to be effective for the synthesis of quinolines.[7] However, most of the methods have significant drawbacks such as low yields of the products, harsh reaction conditions, difficulties in workup, and use of stoichiometric quantities of reagents. Since quinoline derivatives are increasingly useful and important in drugs and pharmaceuticals, the development of a simple, efficient, and environmentally benign protocol is still desirable.

In continuation of our efforts to explore novel synthetic routes to form carbon–carbon and carbon–heteroatom bonds and heterocycles,[8] we studied the efficacy of various reagents (5 mol% as standard) in a model reaction between 2-aminophenyl methyl ketone (1 mmol) and ethyl acetoacetate (EAA, 1.2 mmol) in ethanol at ambient temperature for ten hours (Table 1). To our surprise, $Nd(NO_3)_3·6H_2O$ gave the best yield of quinoline **1** (Table 1, entry 9). The optimum product yield was obtained when a 2-aminophenyl methyl ketone/ethyl acetoacetate ratio of 1:1.2 was used. Ethanol was the best among the solvents tested (MeCN, THF, CH_2Cl_2, EtOH, dioxane, $CHCl_3$). The reaction also proceeded under solvent-free conditions, but the yields were poor compared to those obtained with $Nd(NO_3)_3·6H_2O$ for the specified time. In the absence of catalyst, the product could not be

Table 1 Effect of Different Lewis Acid Catalysts on the Reaction between 2-Aminophenyl Methyl Ketone and Ethyl Acetoacetate



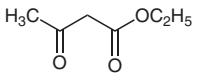
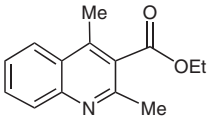
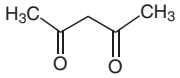
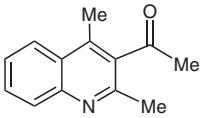
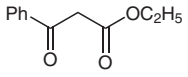
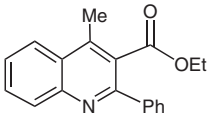
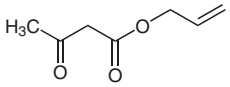
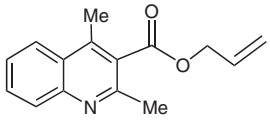
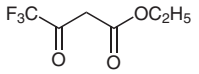
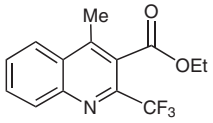
1

Entry	Lewis acid	Yield[a,b] (%)
1	$Pd(acac)_2$	n.r.
2	$Co(acac)_3$	28
3	$VO(acac)_3$	55
4	$Ru(acac)_3$	n.r.
5	$PrCl_3·6H_2O$	58
6	$SmCl_3·6H_2O$	61
7	$YbCl_3·6H_2O$	n.r.
8	$TbCl_3·6H_2O$	62
9	$Nd(NO_3)_3·6H_2O$	78
10	LiBr	18
11	$FeCl_3$	35
12	$La(NO_3)_3·6H_2O$	65
13	TBAB/H_2O	n.r.
14	$RhCl_3$	10
15	$Sm(NO_3)_3·6H_2O$	60

[a] Yield determined by GC.
[b] n.r. = no reaction.

SYNTHESIS 2006, No. 22, pp 3825–3830
Advanced online publication: 09.10.2006
DOI: 10.1055/s-2006-950296; Art ID: P07706SS

Table 2 Neodymium(III) Nitrate Hexahydrate Catalyzed Condensation of Various 1,3-Diketones with 2-Aminoacetophenone

Entry	1,3-Diketone	Product	No	Yield[a] (%)
1			**1**	78
2			**2**	82
3			**3**	70
4			**4**	75
5			**5**	62

[a] Yield of pure, isolated product.

isolated, even after two days. Further, 5 mol% catalyst was sufficient, and the reaction was sluggish when higher or lower catalyst loadings were used. To the best of our knowledge, there are no earlier reports on the use of $Nd(NO_3)_3 \cdot 6H_2O$ as a Lewis acid catalyst in the preparation of quinolines.

Intrigued by the results obtained, we studied the scope of the reaction by investigating the condensation of various 1,3-diketones with 2-aminophenyl methyl ketone under the optimized reaction parameters (Table 2). Among the various 1,3-diketones tested, the order of reactivity towards 2-aminophenyl methyl ketone is as follows: pentane-2,4-dione (Table 2, entry 2) > ethyl acetoacetate (entry 1) > allyl acetoacetate (entry 4) > ethyl benzoylacetate (entry 3) > ethyl 4,4,4-trifluoro-3-oxobutanoate (entry 5).

Table 3 Neodymium(III) Nitrate Hexahydrate Catalyzed Synthesis of Quinolines by Condensation of Various α-Methylene Ketones with Various 2-Aminophenyl Ketones

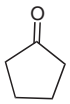
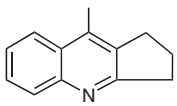
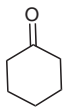
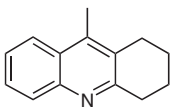
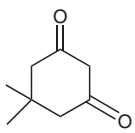
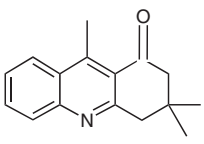
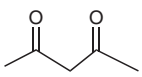
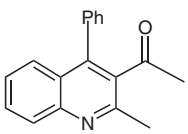
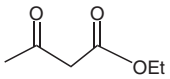
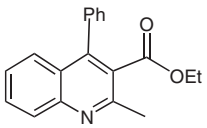
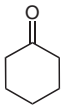
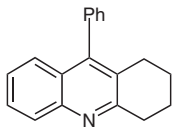
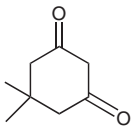
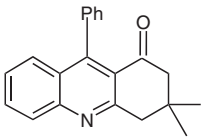
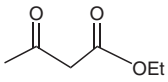
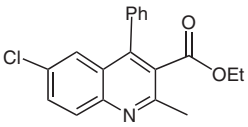
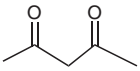
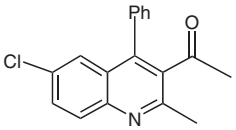
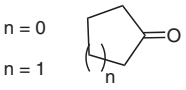
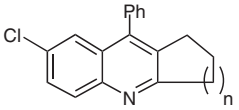
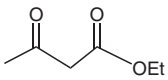
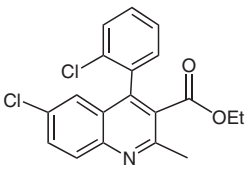
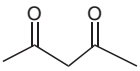
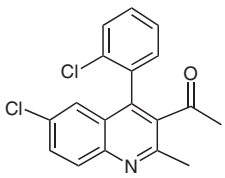
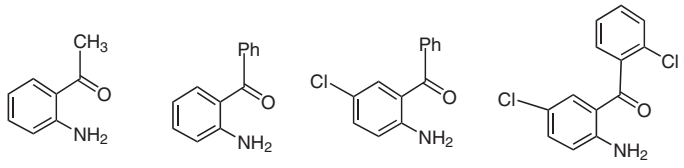
Entry	Ketone	Amine[a]	Product	No	Yield (%)[b]
1		A		**6**	77
2		A		**7**	80
3		A		**8**	85
4		B		**9**	90

Table 3 Neodymium(III) Nitrate Hexahydrate Catalyzed Synthesis of Quinolines by Condensation of Various α-Methylene Ketones with Various 2-Aminophenyl Ketones (continued)

5		B		**10**	92
6		B		**11**	88
7		B		**12**	84
8		C		**13**	85
9		C		**14**	90
10 11		C		**15**	78 82
12		D		**16**	87
13		D		**17**	94

[a] Amines:



A B C D

[b] Yield of isolated, pure product after column chromatography.

We then examined various structurally divergent 2-aminoaryl ketones, e.g. 2-aminophenyl phenyl ketone (B), 2-aminophenyl methyl ketone (A), 2-amino-5-chlorophenyl phenyl ketone (C), and 2-amino-5-chlorophenyl 2-chlorophenyl ketone (D) (Table 3) in the condensation with various α-methylene ketones, e.g. cyclopentanone, cyclohexanone, and 5,5-dimethylcyclohexane-1,3-dione (Table 3). The protocol presented here is equally effective for both cyclic and acyclic ketones. In all cases, reactions were clean, and selfcondensation products, normally observed under basic conditions, were absent. Furthermore, drastic conditions such as high temperatures are not required.

In conclusion, we have demonstrated a mild and efficient synthesis of quinolines, for which $Nd(NO_3)_3·6H_2O$ was used as a novel Lewis acid catalyst. Notable advantages of our protocol includes (a) operational simplicity, (b) good substrate scope, (c) the relatively nontoxic reagents and solvents, and (d) high yields of products.

Melting points were measured on a Buchi R-535 apparatus. IR spectra were determined on a Bruker Vector-22 spectrometer of samples prepared as KBr pellets. ^{1}H NMR spectra (300 MHz) were recorded on a Bruker Avance-300 spectrometer of samples in $CDCl_3$, with chemical shifts (δ) given in ppm relative to TMS as an internal standard. ^{13}C NMR spectra (75.5 MHz) were recorded on a Bruker Avance-300 spectrometer with complete proton decoupling; chemical shifts are reported in ppm relative to the solvent resonance as the internal standard ($CDCl_3$, δ = 77.16). Mass spectra were recorded on a VG 7070H Micromass spectrometer. CHN analyses were recorded on a Vario EL analyzer.

Quinolines 1–17; General Procedure

A mixture of the appropriate 2-aminophenyl ketone (1 mmol), α-methylene ketone (1.2 mmol), and $Nd(NO_3)_3·6H_2O$ (5 mol%) in EtOH (3 mL) was stirred at r.t. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with H_2O and extracted with EtOAc (2 × 10 mL). Evaporation of the solvent followed by purification by column chromatography (silica gel, EtOAc–hexane, 1:9) afforded the corresponding pure quinoline derivative.

Ethyl 2,4-Dimethylquinoline-3-carboxylate (1)

Oil.

IR (KBr): 3070, 2930, 2873, 1725, 1614, 1589, 1214, 1082, 578 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, *J* = 7.17 Hz, 3 H), 2.63 (s, 3 H), 2.68 (s, 3 H), 4.45 (q, *J* = 7.17 Hz, 2 H), 7.46 (t, *J* = 7.6 Hz, 1 H), 7.66 (t, *J* = 7.6 Hz, 1 H), 7.91 (t, *J* = 8.3 Hz, 1 H), 7.99 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9, 154.2, 147.2, 141.1, 129.7 (2 C), 127.8, 126.1, 125.7, 123.6, 61.2, 23.6, 15.5, 14.1.

MS (EI, 70 eV): *m*/*z* = 229 [M$^+$], 186, 158, 125, 77.

Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.12; H, 6.67; N, 6.05.

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

Oil.

IR (KBr): 3068, 2959, 1703, 1614, 1585, 1208, 758 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.57 (s, 3 H), 2.58 (s, 3 H), 2.62 (s, 3 H), 7.53–8.02 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.3, 152.4, 146.7, 138.4, 135.6 (2 C), 129.6, 129.0, 126.2, 123.5, 32.4, 23.3, 15.0.

MS (EI, 70 eV): *m*/*z* = 199 [M$^+$], 158, 125.

Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.32; H, 6.51; N, 7.07.

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

Viscous oil.

IR (KBr): 3046, 2971, 1704, 1612, 1588, 1479, 902 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (q, *J* = 7.03 Hz, 3 H), 2.76 (s, 3 H), 4.15 (q, *J* = 7.03 Hz, 2 H), 7.41–8.16 (m, 9 H).

MS (EI, 70 eV): *m*/*z* = 291 [M$^+$].

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.21; H, 5.92; N, 4.76.

Allyl 2,4-Dimethylquinoline-3-carboxylate (4)

Viscous oil.

IR (KBr): 3032, 2988, 2961, 1624, 1577, 1498, 1267, 1221, 759 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.57 (s, 3 H), 2.63 (s, 3 H), 4.81 (q, *J* = 7.03 Hz, 2 H), 5.41 (d, *J* = 1.56 Hz, 2 H), 6.49 (m, 1 H), 7.56–7.95 (m, 4 H).

MS (EI, 70 eV): *m*/*z* = 241 [M$^+$].

Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.66; H, 6.38; N, 5.82.

Ethyl 4-Methyl-2-(trifluoromethyl)quinoline-3-carboxylate (5)

Viscous oil.

IR (KBr): 2990, 2977, 1688, 1555, 1494, 1454, 1371, 1292, 1221, 754 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, *J* = 7.03 Hz, 3 H), 2.55 (s, 3 H), 4.28 (q, *J* = 7.03 Hz, 2 H), 7.21–8.31 (m, 4 H).

MS (EI, 70 eV): *m*/*z* = 283 [M$^+$].

Anal. Calcd for $C_{14}H_{12}F_3NO_2$: C, 59.37; H, 4.27; N, 4.95. Found: C, 59.18; H, 4.44; N, 5.01.

9-Methyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline (6)

Solid; mp 58–60 °C.

IR (KBr): 3065, 2957, 1613, 908, 751 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.2 (m, 2 H), 2.49 (s, 3 H), 2.99 (t, *J* = 7.5 Hz, 2 H), 3.3 (t, *J* = 6.9 Hz, 2 H), 7.46–8.01 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 147.2, 137.8, 133.7, 128.9, 127.8, 126.9, 125.0, 123.1, 34.8, 29.4, 22.7, 14.6.

MS (EI, 70 eV): *m*/*z* = 183 [M$^+$], 168, 154, 140, 127, 115, 102, 90, 77, 63, 57.

Anal. Calcd for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64. Found: C, 85.17; H, 7.07; N, 7.72.

9-Methyl-1,2,3,4-tetrahydroacridine (7)

Solid; mp 75–77 °C.

IR (KBr): 3068, 2935, 1614, 1581, 1350, 755 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73 (m, 4 H), 2.25 (s, 3 H), 2.61 (t, *J* = 7.6 Hz, 2 H), 2.94 (t, *J* = 7.6 Hz, 2 H), 7.24–7.83 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 145.4, 140.7, 128.4, 127.6, 126.4 (2 C), 124.7, 122.8, 33.9, 26.5, 22.7, 22.3, 12.9.

MS (EI, 70 eV): *m*/*z* = 198 [M$^+$], 125.

Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10. Found: C, 85.19; H, 7.71; N, 7.02.

3,3,9-Trimethyl-3,4-dihydroacridin-1(2*H*)-one (8)

Solid; mp 105–107 °C.

IR (KBr): 2955, 2968, 1682, 1560,1494, 1373, 1280, 1215, 762 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 6 H), 2.67 (s, 2 H), 3.08 (s, 3 H), 3.19 (s, 2 H), 7.57 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1 H), 7.77 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1 H), 8.01 (d, *J* = 8.4 Hz, 1 H), 8.22 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.32, 160.94, 149.56, 148.12, 131.33, 129.09, 127.55, 126.28, 125.41, 124.05, 54.74, 48.43, 31.97, 28.20 (2 C), 15.81.

MS (EI, 70 eV): *m*/*z* = 239 [M$^+$].

Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.21; H, 7.21; N, 5.78.

1-(2-Methyl-4-phenylquinolin-3-yl)ethanone (9)
Solid; mp 114–116 °C.

IR (KBr): 3027, 2960, 1705, 1610, 1569, 1485, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3 H), 2.60 (s, 3 H), 7.25–7.31 (m, 2 H), 7.35 (t, *J* = 8.01 Hz, 1 H), 7.40–7.51 (m, 3 H), 7.55 (d, *J* = 8.1 Hz, 1 H), 7.65 (t, *J* = 8.1 Hz, 1 H), 8.01 (d, *J* = 8.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.6, 153.0 (2 C), 147.0, 144.3, 134.7 (2 C), 129.5 (2 C), 128.4, 128.1, 126.0, 125.6, 124.5, 31.4, 23.3.

MS (EI, 70 eV): *m*/*z* = 261 [M^+], 246, 218, 176, 150, 43.

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.64; H, 5.84; N, 5.32.

Ethyl 2-Methyl-4-phenylquinoline-3-carboxylate (10)
Solid; mp 98–99 °C.

IR (KBr): 3030, 2960, 1700, 1605, 1568, 1482, 905 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.03 Hz, 3 H), 2.80 (s, 3 H), 4.05 (q, *J* = 7.03 Hz, 2 H), 7.35–7.51 (m, 6 H), 7.55 (d, *J* = 8.1 Hz, 1 H), 7.70 (t, *J* = 7.9 Hz, 1 H), 8.06 (d, *J* = 8.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7, 153.6, 147.8, 145.7, 135.7 (2 C), 129.5, 129.1, 128.2, 127.8, 126.4, 126.1, 125.1, 96.1, 68.8, 23.3, 13.6.

MS (EI, 70 eV): *m*/*z* = 291 [M^+], 263, 246, 218, 176, 150.

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.42; H, 5.91; N, 4.88.

9-Phenyl-1,2,3,4-tetrahydroacridine (11)
Solid; mp 140–142 °C.

IR (KBr): 3057, 2945, 1609, 1575, 1480, 1210, 708 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.75–1.85 (m, 2 H), 1.95–2.05 (m, 2 H), 2.60 (t, *J* = 6.71 Hz, 2 H), 3.21 (t, *J* = 6.9 Hz, 2 H), 7.19–7.32 (m, 3 H), 7.41–7.62 (m, 5 H), 8.01 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 146.5, 146.1, 137.3, 129.2, 128.7, 128.5, 128.2, 127.9, 127.5, 126.6, 125.6, 125.2, 34.1, 27.8, 23.1, 22.7.

MS (EI, 70 eV): *m*/*z* = 259 [M^+], 230, 182, 176, 57.

Anal. Calcd for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found: C, 88.02; H, 6.59; N, 5.56.

3,3-Dimethyl-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (12)
Solid; mp 65–66 °C.

IR (KBr): 3060, 2958, 1710, 1601, 1575, 1208, 735 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.20 (s, 6 H), 2.55 (s, 2 H), 3.30 (s, 2 H), 7.11–7.20 (m, 2 H), 7.35–7.49 (m, 5 H), 7.75 (t, *J* = 7.9 Hz, 1 H), 8.05 (d, *J* = 8.1 Hz, 1 H).

MS (EI, 70 eV): *m*/*z* = 301 [M^+], 272, 246, 218, 190.

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.72; H, 6.29; N, 4.71.

Ethyl 6-Chloro-2-methyl-4-phenylquinoline-3-carboxylate (13)
Solid; mp 108 °C.

IR (KBr): 3064, 2983, 1725, 1605, 1224, 907, 732 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.01 Hz, 3 H), 2.73 (s, 3 H), 4.05 (q, *J* = 7.01 Hz, 2 H), 7.32–8.01 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.0, 154.0, 146.1, 145.3, 135.0, 132.3, 131.0, 130.5, 129.2, 128.7, 128.4, 127.6, 125.9, 125.1, 61.4, 23.6, 13.5.

MS (EI, 70 eV): *m*/*z* = 325 [M^+], 296, 280, 252, 217, 189, 176, 149, 123, 109, 88, 71, 57.

Anal. Calcd for $C_{19}H_{16}ClNO_2$: C, 70.05; H, 4.95; N, 4.29. Found: C, 70.09; H, 4.90; N, 4.36.

1-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)ethanone (14)
Solid; mp 149–150 °C.

IR (KBr): 3029, 2960, 1701, 1606, 1567, 1481, 909, 692 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H), 2.66 (s, 3 H), 7.32–7.98 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.9, 153.8 (2 C), 145.8, 142.9, 135.4, 134.5, 132.3, 130.8, 129.8, 129.1, 128.8, 125.8, 124.7, 31.6, 23.6.

MS (EI, 70 eV): *m*/*z* = 295 [M^+], 280, 252, 217, 189, 176, 149, 109, 94, 75.

Anal. Calcd for $C_{18}H_{14}ClNO$: C, 73.10; H, 4.77; N, 4.74. Found: C, 73.01; H, 4.82; N, 4.66.

7-Chloro-9-phenyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline (15, n = 1)
Solid; mp 104–106 °C.

IR (KBr): 3060, 2958, 1606, 1487, 828, 715 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.12 (m, 2 H), 2.87 (t, *J* = 7.2 Hz, 2 H), 3.19 (t, *J* = 7.01 Hz, 2 H), 7.32–7.98 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7, 146.3, 141.8, 135.9, 134.3, 131.2, 130.3, 129.0, 128.6, 128.2, 126.9, 124.4, 35.0, 30.2, 23.3.

MS (EI, 70 eV): *m*/*z* = 279 [M^+], 244, 202, 167, 121, 114, 94, 87, 75, 63.

Anal. Calcd for $C_{18}H_{14}ClN$: C, 77.28; H, 5.04; N, 5.01. Found: C, 77.19; H, 4.94; N, 4.86.

7-Chloro-9-phenyl-1,2,3,4-tetrahydroacridine (15, n = 2)
Solid; mp 163 °C.

IR (KBr): 3060, 2944, 1604, 1572, 1481, 1215, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.55 (m, 2 H), 1.59 (m, 2 H), 2.56 (t, *J* = 6.5 Hz, 2 H), 3.30 (t, *J* = 7.01 Hz, 2 H), 7.22–8.02 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 145.8, 144.8, 136.5, 131.3, 130.2, 129.5, 129.3, 129.1, 128.9, 128.2, 127.5, 124.6, 34.3, 28.2, 23.1.

MS (EI, 70 eV): *m*/*z* = 293 [M^+], 278, 258, 242, 230, 201, 189, 176, 150, 89, 77.

Anal. Calcd for $C_{19}H_{16}ClN$: C, 77.68; H, 5.49; N, 4.77. Found: C, 77.59; H, 5.34; N, 4.68.

Ethyl 6-Chloro-4-(2-chlorophenyl)-2-methylquinoline-3-carboxylate (16)
Solid; mp 115–117 °C.

IR (KBr): 3061, 2979, 1725, 1602, 905, 729 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.95–0.98 (m, 3 H), 2.81 (s, 3 H), 4.06–4.08 (m, 2 H), 7.27–7.55 (m, 6 H), 8.02 (d, *J* = 9.3 Hz, 1 H).

MS (EI, 70 eV): *m*/*z* = 360.

Anal. Calcd for $C_{19}H_{15}Cl_2NO_2$: C, 70.05; H, 4.95; N, 4.29. Found: C, 70.09; H, 4.90; N, 4.36.

1-[6-Chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl]ethanone (17)

Solid; mp 138–140 °C.

IR (KBr): 3025, 2978, 1701, 1604, 1570, 1484, 911, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3 H), 2.71 (s, 3 H), 7.23–7.28 (m, 2 H), 7.40–7.67 (m, 4 H), 8.01 (d, *J* = 9.2 Hz, 1 H).

MS (EI, 70 eV): *m*/*z* = 212.

Anal. Calcd for $C_{18}H_{13}Cl_2NO$: C, 65.47; H, 3.97; N, 4.24. Found: C, 65.36; H, 4.04; N, 4.31.

Acknowledgment

R.V. thanks DIICT, Dr. J. S. Yadav, and the Council of Scientific Industrial Research (CSIR, India) for financial support.

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