A multicomponent reaction of acetals for the preparation of quinolines

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A straightforward, mild, one-pot method has been found for the preparation of quinolines via a multi-component reaction using acetals or cyclic acetals, aromatic amines and alkynes catalysed by $Bi(OTf)_3$. It gives good yields under mild conditions. This approach has been successfully applied for the synthesis of a range of quinolines with a variety of functional groups.

Keywords: quinolines, multicomponent reaction, acetals, amines, alkynes

Quinolines are an important family of heterocyclic compounds which include a number of biologically active compounds.[1] Numerous synthetic methods have been developed for the synthesis of the quinoline ring construction.[1,2] Friedländer annulation is the most simple, straightforward, and widely used approach.[3–5] Drawbacks associated with this type of reaction are the low stability of 2-aminobenzaldehyde. Povarov reaction[6] is another well-established protocol involving the coupling of *N*-aryl aldimines with alkynes or alkenes catalysed by either protic[7] or Lewis acids.[8] Although these approaches provide efficient access to quinolines, many starting materials are not readily available.

In view of the fact that imines can be formed *in situ* from aldehydes and amines,[9] a three-component Povarov reaction involving aldehydes, amines, and alkynes has been established for constructing quinoline nucleus.[6,10] Compared to stepwise procedures, multicomponent reactions (MCRs) exhibit advantages since several bonds are formed in a one-pot operation and the formation of waste is minimised.

Acetals are extensively used as protecting groups[11–13] and prove to be a versatile function able to undergo a wide range of reactions such as the displacement of one alkoxy group in acetals by various nucleophiles.[14–16] However, MCRs including acetals are quite scarce. As part of our continuing effort on extending the application of acetals as a function in the area of organic synthesis, we report here the first reaction of acetals with alkynes and anilines to furnish quinolines (Scheme 1).

This mild reaction of acetals was observed during our investigation on an $InCl_3$-catalysed A^3-reaction of acetals with alkynes and amines, *via* a one-pot process for preparing propargylamines. Instead of the anticipated propargylamine product, a quinoline derivative was formed in 38% isolated yield when the reaction was conducted in toluene at 110 °C. The valuable results prompted us to establish a mild protocol for the construction of the quinoline ring starting from acetals.

Initially, the reaction of aniline, benzaldehyde dimethyl acetal and phenylacetylene was first conducted with $InCl_3$ (10 mol%) in CH_3CN solution. It failed at room temperature but the anticipated 2, 4-diphenylquinoline was obtained in 36% yield after the solution was heated to reflux. To improve the yield, a variety of reaction parameters were optimised. Catalyst screening was first executed and disclosed that $Bi(OTf)_3$ was the most efficient one among $InCl_3$, $FeCl_3$, $BiCl_3$, $AlCl_3$, $SnCl_2$, CuCl, CuBr, CuI and I_2 (Table 1, entries 1–9). Both CuOTf and I_2 had slightly lower activity to afford quinoline products

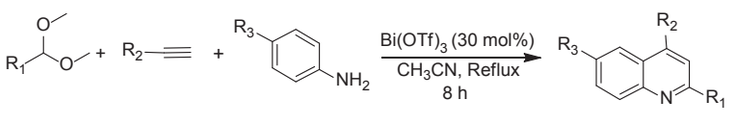
Table 1 Results of screening solvents and Lewis acids[a]

Entry	Catalyst	Solvent	Temp./°C	Time/h	Yield/%[b]
1	$InCl_3$	CH_3CN	82	8	36
2	$Bi(OTf)_3$	CH_3CN	82	8	73
3	$FeCl_3$	CH_3CN	82	6	54
4	$BiCl_3$	CH_3CN	82	10	47
5	$AlCl_3$	CH_3CN	82	9	60
6	$SnCl_2$	CH_3CN	82	9	40
7	CuCl	CH_3CN	82	8	56
8	CuBr	CH_3CN	82	8	59
9	CuI	CH_3CN	82	10	24
10	CuOTf	CH_3CN	82	8	63
11	I_2	CH_3CN	82	10	63
12	$Bi(OTf)_3$	CH_3NO_2	102	8	69
13	$Bi(OTf)_3$	EtOH	80	9	26
14	$Bi(OTf)_3$	1, 4-dioxane	102	8	55
15	$Bi(OTf)_3$	DCE	83	9	67
16	$Bi(OTf)_3$	THF	67	9	15
17	$Bi(OTf)_3$	Toluene	110	8	70
18	$Bi(OTf)_3$	CH_2Cl_2	40	9	25

[a]Reaction conditions: phenylacetylene (1.5 mmol), benzaldehyde dimethyl acetal (1.2 mmol), aniline (1.0 mmol), catalyst (0.30 mmol), solvent (4.0 mL), reflux.
[b]Isolated yields after flash chromatography.

(Table 1, entries 10–11). Solvent selection showed that this multicomponent process proceeded with high efficiency in refluxing CH_3CN solution (Table 1, entry 2, yield 73%). In refluxing toluene solution, the yield was slightly lower (Table 1, entry 17, yield 70%). In the solution of THF or EtOH, the yield was much lower (Table 1, entries 13 and 16, yield < 26%). Both proved to be unsuitable for this transformation. The much lower yield in dichloromethane than in 1, 2-dichloroethane is possibly due to the lower reaction temperature (Table 1, entries 15 and 18; 25% *versus* 67%). It is important to note that this is an inexpensive, regioselective, and efficient approach to 2, 4-substituted quinolines from the simple and readily available starting materials.

Using the optimal conditions, a range of acetals were examined for this three component one-pot procedure. As described in Table 2, all the acetals tested were smoothly transformed to the corresponding 2,4-disubstituted quinolines in good yields. Moreover, electronic variation in the aryl acetals alters the efficiency of the reaction. Electron donating groups, like the *p*-methoxy and *p*-methyl, led to lower yields (Table 2, entries 2 and 3 *versus* 1). A weak electron-withdrawing substituents, such as *p*-F, *p*-Cl, *p*-Br, led to slightly lower



Scheme 1 A multicomponent reaction of acetals for quinolines.

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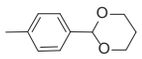
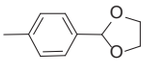
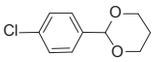
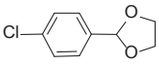
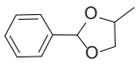
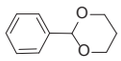
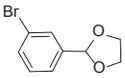
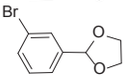
Table 2 Three-component reaction of acetals with phenylacetylene and amines to form quinolines[a]

Entry	Quinoline 2-substituent(acetal)	Quinoline 6-substituent(amine)	Yield/%[b]
1	C_6H_5	H	73
2	*p*-$CH_3OC_6H_4$	H	55
3	*p*-$CH_3C_6H_4$	H	59
4	*p*-FC_6H_4	H	67
5	*p*-ClC_6H_4	H	72
6	*p*-BrC_6H_4	H	64
7	*p*-$NO_2C_6H_4$	H	56
8	*m*-$NO_2C_6H_4$	H	52
9		H	59
10		H	57
11		H	68
12		H	64
13		H	61
14		H	55
15		H	63
16		CH_3	59
17		H	0

[a]Reaction conditions: phenylacetylene (1.5 mmol), acetals (1.2 mmol), amines (1.0 mmol), $Bi(OTf)_3$ (0.197 g, 0.30 mmol), acetonitrile (4.0 mL), reflux, 8 h.
[b]Isolated yields after flash chromatography.

yields (Table 2, entries 4–6 *versus* 1), but higher than those for electron donating groups (Table 2, entries 4–6 *versus* 2 and 3). With strong electron-withdrawing groups like *m*-NO_2 and *p*-NO_2 the yields were also good, but less than in those associated with weak electron-withdrawing groups (Table 2, entries 7 and 8 *versus* 4–6). Compared to the trace amount of quinoline product given by *m*-nitrobenzaldehyde,[17] our process gave the expected product at quite good yield (Table 2, entry 8, yield 52%). Thus these results validate an efficient procedure from acetals to build 2, 4-diarylquinoline nucleus.[2,10,17]

The substrate versatility of this mild protocol was further demonstrated by cyclic acetals, which are more stable than their acyclic acetals. As shown in Table 2, both five- and six-membered-ring acetals showed similar reactivity to acyclic acetals undergoing this mild MCR to give the corresponding quinolines with good yields (Table 2, entries 9–15). In some cases, the yields given by acetals were nearly the same as those associated with the corresponding aldehydes.[10,18] Halogen substituents in acetals show slight reduction in yield in this

Table 3 Three-component reaction of acetals with alkynes and amines to form quinolines[a]

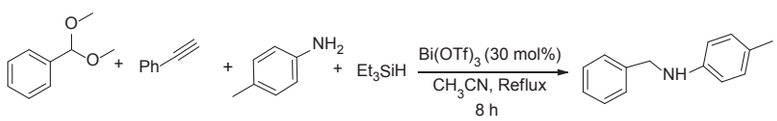
Entry	Quinoline 2-substituent (acetal)	Quinoline 4-substituent (alkyne)	Quinoline 6-sbustituent (amine)	Yield/%[b]
1	C_6H_5	C_6H_5	CH_3O	63
2	C_6H_5	C_6H_5	CH_3	66
3	C_6H_5	C_6H_5	Cl	74
4	C_6H_5	C_6H_5	NO_2	61
5	*p*-ClC_6H_4	C_6H_5	NO_2	67
6	C_6H_5	C_6H_5	COOEt	61
7	C_6H_5	*n*-hexyl	CH_3	35
8	C_6H_5	COOMe	H	35
9	C_6H_5	*p*-FC_6H_4	H	70
10	C_6H_5	*p*-$CH_3C_6H_4$	H	65
11	C_6H_5	*p*-$CH_3OC_6H_4$	H	59
12	C_6H_5	Diphenylacetylene	H	0

[a]Reaction conditions: alkyne (1.5 mmol), acetal (1.2 mmol), amine (1.0 mmol), $Bi(OTf)_3$ (0.197 g, 0.30 mmol), acetonitrile (4.0 mL), reflux, 8 h.
[b]Isolated yields after flash chromatography.

transformation (Table 2, entries 3–5, 9 and 10). But in terms of alkyl acetals, the yield was zero (Table 2, entry 17).

In term of aniline substrates, as shown in Table 3, both electron-deficient and electron-sufficient aryl amines, such as *p*-methoxy, acyl and *p*-nitro anilines, exhibited similar efficiency and gave the corresponding products with good yields (Table 3, entries 1–6). Aryl alkynes gave the products in higher yields than alkyl alkenes (Table 3, entries 7–11). When 1-octyne or methyl propiolate was employed in this process, the desired quinoline product was formed in a much lower yield (Table 3, entries 7 and 8). The yield associated with 4-fluorophenylacetylene was quite good (70%) and higher than those with *p*-methoxy or *p*-methylphenylacetylene (Table 3, entry 9 *versus* 10 and 11). A strong electron-donating *p*-methoxy group led to a lower yield than the weak electron-donating group of *p*-methyl (Table 3, entries 10 and 11). But in terms of diphenylacetylene, the yield was zero (Table 3, entry 12). Aldehydes gave the quinoline product in yield and a [4+2] pathway was proposed for the coupling of aldehyde, alkyne and amines. Probably a different mechanism takes place as acetals are used in this reaction.

To elucidate the reaction pathway, we hoped to intercept the reaction intermediate. Yang and coworkers[19] demonstrated that [In–H] generated in the $InCl_3/Et_3SiH/MeOH$ system is an active agent for reductive amination of aldehydes with various amines. Accordingly, we introduced Et_3SiH into this reaction system in an attempt to trap an iminium ion. Under our standard reaction conditions, Et_3SiH (2.0 equiv.) was added to the reaction solution of benzaldehyde dimethyl acetal, aniline, and phenylacetylene. Indeed, only *N*-benzyl-4-methylaniline (the reductive amination product) was obtained in 91% yield (Scheme 2). The formation of *N*-benzyl-4-methylaniline showed that benzaldehyde dimethyl acetal was first transformed into an iminium ion with aniline and subsequently reduced by Et_3SiH *in situ*. The direct reductive amination of acetals with amines could occur *in situ* in the presence of $Bi(OTf)_3$–Et_3SiH. These experimental findings provided corroborative evidence that this acetal protocol proceeds *via* the formation of an iminium ion as an intermediate.[20,21]



Scheme 2 The reductive amination product.

In conclusion, we have described the first MCR of acetals *via* activating both C–O and C–H bonds. Both alkyloxy groups of acetals were displaced with amines and alkynes *in situ* to give quinolines. Besides the advantages of MCR, our protocol also provides methods to reduce waste and synthetic steps due to eliminating deprotection procedure with regards to protecting groups. The first MCR of acetals might broadly expand the role of acetals apart from use as a masking group. The scope, mechanism, stereoselectivity, and synthetic applications of this reaction are under investigation.

Experimental

Reactions were performed under air. The materials were used as purchased. Unless otherwise stated, all solvents and reagents were commercially available and used as purchased without further purification. Reactions were monitored by thin-layer chromatography using gel F 254 plates. The silica gel (300–400 meshes) was used for column chromatography, and the distillation range of petroleum ether was 60–90 °C. NMR spectra was recorded in $CDCl_3$ on either a Varian 400 MHz or a Bruker 400 MHz Fourier-transform spectrometer. Chemical shifts were reported in ppm referenced to TMS or the $CHCl_3$ solvent residual peak at 7.26 ppm for ^1H and 77.23 ppm for ^{13}C.

Preparation of quinolines

The acetal (1.2 mmol), aromatic amine (1.0 mmol), alkyne (1.5 mmol), and $Bi(OTf)_3$ (0.197 g, 0.3 mmol) were added to a flask (25 mL), followed by the addition of acetonitrile (4.0 mL) under air. The mixture was stirred under reflux and monitored by TLC. The solution was then cooled to room temperature, diluted with dichloromethane (5 mL), and washed with brine. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether) to afford the desired product.

2,4-Diphenylquinoline: White solid, m.p. 113–114 °C (lit.[22] 111–112 °C); yield 73% (Table 2, entry 1), 61% (Table 2, entry 13) and 55 (Table 2, entry 14); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.83 (s, 1H), 7.74 (t, *J* = 8.3 Hz, 1H), 7.60–7.44 (m, 9H).

2-(4-Methoxyphenyl)-4-phenylquinoline: White solid, m.p. 77–78 °C (lit.[23] 78–79 °C); yield 55% (Table 2, entry 2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 8.9 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.69 (s, 1H), 7.66–7.61 (m, 1H), 7.50–7.41 (m, 5H), 7.39–7.33 (m, 1H), 6.96 (d, *J* = 10.7 Hz, 2H), 3.80 (s, 3H).

4-Phenyl-2-(p-tolyl)-quinoline: White solid, m.p. 104–105 °C (lit.[23] 95–96 °C); yield 59% (Table 2, entry 3), 59% (Table 2, entry 9) and 57% (Table 2, entry 10); ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 7.4 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.81 (s, 1H), 7.76–7.69 (m, 1H), 7.60–7.43 (m, 6H), 7.33 (d, *J* = 7.8 Hz, 2H), 2.44 (s, 3H).

2-(4-Fluorophenyl)-4-phenylquinoline: White solid, m.p. 64–65 °C (lit.[23] 63–64 °C); yield 67% (Table 2, entry 4); ^1H NMR (400 MHz, $CDCl_3$) δ 8.16–8.08 (m, 3H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.70–7.63 (m, 2H), 7.53–7.33 (m, 6H), 7.13 (t, *J* = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.02, 161.54, 154.73, 148.31, 147.72, 137.27, 134.77, 134.74, 128.98, 128.61, 128.50, 128.43, 128.35, 127.58, 127.44, 125.36, 124.64, 117.94, 114.84, 114.62.

2-(4-Chlorophenyl)-4-phenylquinoline: White solid, m.p. 104–105 °C (lit.[23] 104–105 °C); yield 72% (Table 2, entry 5), 68% (Table 2, entry 11) and 64% (Table 2, entry 12). ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.3 Hz, 1H), 8.19 (d, *J* = 8.6 Hz, 2H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.81–7.75 (m, 2H), 7.61–7.56 (m, 5H), 7.52 (dd, *J* = 11.0, 4.3 Hz, 3H).

2-(4-Bromophenyl)-4-phenylquinoline: White solid, m.p. 121–122 °C (lit.[23] 111–112 °C); yield 64% (Table 2, entry 6); ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.71–7.64 (m, 2H), 7.60–7.55 (m, 2H), 7.49–7.39 (m, 6H).

2-(4-Nitrophenyl)-4-phenylquinoline: Yellow solid, m.p. 160–161 °C (lit.[23] 156–157 °C); yield 56% (Table 2, entry 7); ^1H NMR (400 MHz, $CDCl_3$) δ 8.32–8.24 (m, 4H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.76 (s, 1H), 7.72–7.66 (m, 1H), 7.52–7.41 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.01, 148.83, 147.76, 147.29, 144.40, 136.87, 129.29, 129.02, 128.47, 127.69, 127.27, 126.27, 125.13, 124.74, 122.96, 118.04.

2-(3-Nitrophenyl)-4-phenylquinoline: Yellow solid, m.p. 153–154 °C; yield 52% (Table 2, entry 8); ^1H NMR (400 MHz, $CDCl_3$) δ 9.00 (t, *J* = 1.9 Hz, 1H), 8.52 (d, *J* = 7.8 Hz, 1H), 8.24 (dd, *J* = 8.2, 2.2 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.72 (dd, *J* = 11.1, 4.2 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.52–7.44 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.92, 148.95, 147.82, 147.73, 140.25, 136.92, 132.32, 129.21, 129.00, 128.76, 128.50, 127.70, 127.67, 126.09, 125.12, 124.76, 122.89, 121.40, 117.64. HRMS (ESI) calcd for $C_{21}H_{15}N_2O_2$ $[M+H^+]$: 327.11280, found 327.11273.

2-(3-Bromophenyl)-4-phenylquinoline[2]: White solid, m.p. 91–92 °C; yield 63% (Table 2, entry 15); ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.69–7.63 (m, 2H), 7.52–7.38 (m, 7H), 7.31 (d, *J* = 9.1 Hz, 1H).

2-(3-Bromophenyl)-6-methyl-4-phenylquinoline[2]: Yellow solid, m.p. 94–95 °C; yield 59% (Table 2, entry 16); ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.01 (dd, *J* = 16.8, 8.2 Hz, 2H), 7.62 (s, 1H), 7.55 (s, 1H), 7.49–7.41 (m, 7H), 7.28–7.24 (m, 1H), 2.37 (s, 3H).

6-Methoxy-2, 4-diphenylquinoline: Yellow solid, m.p. 119–120 °C (lit.[24] 108–110 °C); yield 63% (Table 3, entry 1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.11–8.05 (m, 3H), 7.69 (s, 1H), 7.47 (m, 7H), 7.38–7.29 (m, 2H), 7.11 (d, *J* = 2.6 Hz, 1H), 3.72 (s, 3H).

6-Methyl-2, 4-diphenylquinoline: White solid, m.p. 128–129 °C (lit.[25] 111 °C); yield 66% (Table 3, entry 2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25–8.17 (m, 3H), 7.82 (s, 1H), 7.69 (s, 1H), 7.63–7.53 (m, 8H), 7.49 (t, *J* = 6.6 Hz, 1H), 2.51 (s, 3H).

6-Chloro-2, 4-diphenylquinoline: White solid, m.p. 129–130 °C (lit.[22] 130–132 °C); yield 74% (Table 3, entry 3); ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (t, *J* = 8.9 Hz, 3H), 7.91–7.86 (m, 2H), 7.70 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.62–7.49 (m, 8H).

6-Nitro-2, 4-diphenylquinoline: Yellow solid, m.p. 200–201 °C (lit.[26] 264 °C); yield 61% (Table 3, entry 4); ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 2.4 Hz, 1H), 8.41 (dd, *J* = 9.2, 2.4 Hz, 1H), 8.25 (d, *J* = 9.2 Hz, 1H), 8.17 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.90 (s, 1H), 7.56–7.44 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.01, 150.24, 150.01, 144.36, 137.46, 135.85, 130.73, 129.42, 128.42, 128.30, 128.11, 128.02, 126.81, 123.78, 122.05, 121.89, 119.70.

2-(4-Chlorophenyl)-6-nitro-4-phenylquinoline[18]: Yellow solid, m.p. 118–119 °C; yield 67% (Table 3, entry 5); ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.41 (d, *J* = 9.2 Hz, 1H), 8.23 (d, *J* = 9.2 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 2H), 7.86 (s, 1H), 7.49 (dt, *J* = 22.6, 7.5 Hz, 7H).

Ethyl-2, 4-diphenylquinoline-6-carboxylate: White solid, m.p. 133–134 °C; yield 61% (Table 3, entry 6); ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.32 (t, *J* = 8.2 Hz, 2H), 8.23 (d, *J* = 7.0 Hz, 2H), 7.89 (s, 1H), 7.65–7.47 (m, 7H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.47, 158.80, 150.79, 137.81, 130.33, 130.05, 129.70, 129.25, 129.06, 128.95, 128.26, 127.88, 125.13, 120.12, 109.89, 61.40, 14.45. HRMS (ESI) calcd for $C_{24}H_{20}NO_2$ $[M+H^+]$: 354.14886, found 354.14886.

4-Hexyl-6-methyl-2-phenylquinoline: White solid, m.p. 67–68 °C; yield 35% (Table 3, entry 7); ^1H NMR (400 MHz, $CDCl_3$) δ 8.10–8.03 (m, 2H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.70 (s, 1H), 7.59 (s, 1H), 7.44 (dd, *J* = 11.9, 8.2 Hz, 3H), 7.36 (t, *J* = 7.3 Hz, 1H), 3.07–2.95 (m, 2H), 2.50 (s, 3H), 1.73 (m, 2H), 1.40 (dd, *J* = 14.8, 7.1 Hz, 2H), 1.28 (t, *J* = 6.8 Hz, 4H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.19, 147.50, 145.99, 139.08, 134.67, 130.32, 129.15, 127.92, 127.70, 126.43, 125.46, 121.33, 117.66, 31.48, 30.66, 29.05, 28.41, 21.59, 20.95, 13.07. HRMS (ESI) calcd for $C_{22}H_{26}N$ $[M+H^+]$: 304.20598, found 304.20596.

Methyl-2-phenylquinoline-4-carboxylate: White solid, m.p. 57–58 °C; yield 35% (Table 3, entry 8); ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.88–7.79 (m, 1H), 7.65 (d, *J* = 6.9 Hz, 2H), 7.48 (d, *J* = 7.3 Hz, 3H), 7.26 (s, 1H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.41, 158.08, 148.42, 139.38, 131.77, 129.56, 128.79, 128.63, 128.31, 127.39, 125.88, 125.12, 52.53. HRMS (ESI) calcd for $C_{17}H_{14}NO_2$ $[M+H^+]$: 264.10191, found 264.10165.

4-(4-Fluorophenyl)-2-phenylquinoline: Light yellow solid, m.p. 82–83 °C (lit.[27] 82–84 °C); yield 70% (Table 3, entry 9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J*=8.8 Hz, 1H), 8.10 (dd, *J*=8.3, 1.2 Hz, 2H), 7.77 (d, *J*=8.4 Hz, 1H), 7.70 (s, 1H), 7.68–7.62 (m, 1H), 7.47–7.35 (m, 6H), 7.16 (dd, *J*=9.9, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.10, 160.63, 155.85, 147.78, 147.03, 138.50, 133.32, 133.28, 130.26, 130.18, 129.18, 128.58, 128.37, 127.82, 126.53, 125.43, 124.69, 124.31, 118.35, 114.74, 114.52. HRMS (ESI) calcd for$C_{21}H_{15}FN$ [M+H$^+$]: 300.11830, found 300.11816.

2-Phenyl-4-(p-tolyl)quinoline: Light yellow oily liquid; yield 65% (Table 3, entry 10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J*=8.5 Hz, 1H), 8.10 (d, *J*=7.2 Hz, 2H), 7.85 (d, *J*=8.3 Hz, 1H), 7.72 (s, 1H), 7.66–7.61 (m, 1H), 7.43 (t, *J*=7.3 Hz, 2H), 7.37 (d, *J*=8.1 Hz, 4H), 7.27 (d, *J*=7.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.86, 148.16, 147.79, 138.70, 137.28, 134.43, 129.06, 128.44, 128.40, 128.25, 127.78, 126.54, 125.18, 124.84, 124.66, 118.29, 20.28. HRMS (ESI) calcd for $C_{22}H_{18}N$ [M+H$^+$]: 296.14338, found 296.14307.

4-(4-Methoxyphenyl)-2-phenylquinoline: White solid, m.p. 85–86 °C (lit.[28] 101.4–102.0 °C); yield 59% (Table 3, entry 11); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J*=8.4 Hz, 1H), 8.10 (d, *J*=7.1 Hz, 2H), 7.86 (d, *J*=8.4 Hz, 1H), 7.70 (s, 1H), 7.65–7.60 (m, 1H), 7.40 (m, 6H), 6.99 (d, *J*=8.7 Hz, 2H), 3.81 (s, 3H).

N-Benzyl-4-methylaniline[29]: Light yellow oily liquid; yield 91% (Scheme 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.35 (m, 4H), 7.34–7.24 (m, 1H), 7.03 (d, *J*=7.9 Hz, 2H), 6.61 (d, *J*=8.3 Hz, 2H), 4.34 (s, 2H), 3.97 (br s, 1H), 2.28 (s, 3H).

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Reference

1 A.R. Katritzky and C.W. Rees, *Comprehensive heterocyclic chemistry*, Pergamon Press, Oxford, 1984.
2 F. Xiao, Y. Chen, Y. Liu and J. Wang, *Tetrahedron*, 2008, **64**, 2755.
3 S.V. Ryabukhin, V.S. Naumchik, A.S. Plaskon, O.O. Grygorenko and A.A. Tolmachev, *J. Org. Chem.*, 2011, **76**, 5774.
4 W. Luo, Q. Mu, W. Qiu, T. Liu, F. Yang, X. Liu and J. Tang, *Tetrahedron*, 2011, **67**, 7090.
5 S. Atechian, N. Nock, R.D. Norcross, H. Ratni, A.W. Thomas, J. Verron and R. Masciadri, *Tetrahedron*, 2007, **63**, 2811.
6 V.V. Kouznetsov, *Tetrahedron*, 2009, **65**, 2721.
7 R. Baudelle, P. Melnyk, B. Déprez and A. Tartar, *Tetrahedron*, 1998, **54**, 4125.
8 J.M. Urbina, J.C.G. Cortes, A. Palma, S.N. Lopez, S.A. Zacchino, R.D. Enriz, J.C. Ribas and V.V. Kouznetzov, *Bioorgan. Med. Chem.*, 2000, **8**, 691.
9 Y. Zhang, P. Li, M. Wang and L. Wang, *J. Org. Chem*., 2009, **74**, 4364.
10 K. Cao, F.M. Zhang, Y.Q. Tu, X.T. Zhou and C.A. Fan, *Chem. Eur. J.*, 2009, **15**, 6332.
11 M.A. Kumar, P. Swamy, M. Naresh, M.M. Reddy, C.N. Rohitha, S. Prabhakar, A.V.S. Sarma, J.R.P. Kumar and N. Narender, *Chem. Commun.*, 2013, **49**, 1711.
12 Y. Liu, B. Jiang, W. Zhang and Z. Xu, *J. Org. Chem.*, 2013, **78**, 966–980.
13 M. Yamamoto, S. Nakaoka, Y. Ura and Y. Kataoka, *Chem. Commun.*, 2012, **48**, 1165.
14 S. Ito, A. Hayashi, H. Komai, H. Yamaguchi, Y. Kubota and M. Asami, *Tetrahedron*, 2011, **67**, 2081.
15 P. Maity, H.D. Srinivas, M.P. Watson, *J. Am. Chem. Soc.*, 2011, **133**, 17142.
16 M. Zhang, Y. Wang, Y. Yang and X. Hu, *Adv. Synth. Catal*., 2012, **354**, 981.
17 J. Tang, L. Wang, D. Mao, W. Wang, L. Zhang, S. Wu and Y. Xie, *Tetrahedron*, 2011, **67**, 8465.
18 S.K. Guchhait, K. Jadeja and C. Madaan, *Tetrahedron Lett*., 2009, **50**, 6861.
19 O.Y. Lee, K.L. Law, C.Y. Ho and D. Yang, *J. Org. Chem.*, 2008, 73, 8829.
20 M.H.S.A. Hamid, C.L. Allen, G.W. Lamb, A.C. Maxwell, H.C. Maytum, A.J.A. Watson and J.M.J. Williams, *J. Am. Chem. Soc*., 2009, **131**, 1766.
21 G.W. Lamb, A.J.A.Watson, K.E. Jolley, A.C. Maxwell and J.M.J. Williams, *Tetrahedron Lett.*, 2009, **50**, 3374.
22 R. Martinez, D.J. Ramon and M. Yus, *Eur. J. Org. Chem.*, 2007, **10**, 1599.
23 H.M. Wang, R.S. Hou, H.D. Du, I.J. Kang and L.C. Chen, *Heterocycles*, 2011, **83**, 331.
24 Q.L. Dong, G.S. Liu, H.B. Zhou, L. Chen and Z.J. Yao, *Tetrahedron Lett.*, 2008, **49**, 1636.
25 R.P. Korivi and C.H. Cheng, *J. Org. Chem.*, 2006, 71, 7079.
26 R. Sarma and D. Prajapati, *Synlett*, 2008, **19**, 3001.
27 C.S. Jia, Z. Zhang, S.J. Tu and G.W. Wang, *Org. Biomol. Chem*., 2006, **4**, 104.
28 S. Miyajima, K. Ito, Isao K. and Choji K. *Nippon Kagaku Kaishi*, 1979, 11, 1514.
29 F. Nador, Y. Moglie, A. Ciolino, A. Pierini, V. Dorn, M. Yus, F. Alonso and G. Radivoy, *Tetrahedron Lett*., 2012, **53**, 3156.