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$RuCl_2(dmso)_4$ Catalyzes the Solvent-Free Indirect Friedländer Synthesis of Polysubstituted Quinolines from Alcohols

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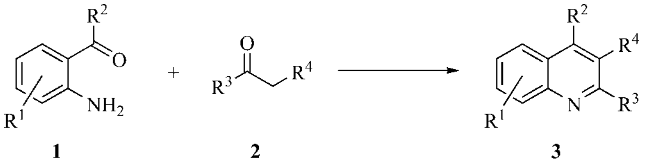
The first synthesis of polysubstituted quinoline derivatives from aromatic or aliphatic alcohols with $RuCl_2(dmso)_4$ as catalyst under solvent-free conditions is described. The reaction involves the in situ oxidation of alcohols to the corresponding carbonyl compounds through a hydrogen-transfer, followed by a Friedländer annulation process. The whole process is a mild, efficient, selective, and high-yielding single-step procedure.

Introduction

The presence of quinoline scaffolds in the frameworks of various pharmacologically active compounds, as well as in various natural products, has spurred on the development of many different methodologies for their synthesis.[1] Among their different applications,[2] functionalized quinolines are in widespread use as a result of their anti-malarial,[3] anti-inflammatory,[4] anti-asthmatic,[5] anti-bacterial,[6] and anti-hypersensitive activities.[7] Several different strategies for the preparation of substituted quinolines are known, with the Friedländer annulation being the most simple, straightforward, and widely used approach (Scheme 1).[8] This type of reaction is usually performed either by heating an aqueous or alcoholic solution of reactants at reflux in the presence of base, or by heating the above reagents at high temperature (up to 250 °C) in the absence of catalyst. 2-Aminophenyl ketone or aldehyde derivatives **1** are used as the electrophilic partner and different carbonyl compounds possessing acidic α-hydrogen atoms **2** are employed as source of the nucleophile. Under thermal or base catalysis conditions, however, aminobenzophenone (**1a**: R^1 = H, R^2 = Ph) failed to react with simple ketones **2**.[9] This limitation has been overcome, though, by the use of acid catalysts such as Brønsted acids[10] (polyphosphoric, sulfamic, or *p*-toluenesulfonic acid) or Lewis acids[11] [$AuCl_3$, $Y(OTf)_3$, $ZnCl_2$, $Ag_3PW_{12}O_{40}$, $FeCl_3$, or $Mg(ClO_4)_2$]. Nevertheless, most of the synthetic approached reported so far suffer from the need for high temperatures or harsh reaction conditions, low yields, use of hazardous and often expensive catalysts, and problems associated with the storage and stability of carbonyl reagents. Moreover, this reaction is usually carried out in polar solvents, resulting in tedious workup procedures.



Scheme 1. Friedländer annulation.

A new methodology using 2-aminobenzyl alcohol as source of electrophilic partner **1** in the Friedländer annulation has recently been proposed as an alternative, and some of the problems mentioned above, such as the instability of the corresponding aminobenzaldehyde, have been overcome in this way. The reaction is initiated by hydride abstraction from the benzyl alcohol by the catalysts, followed by imine formation and a final aldol-ring closing process under basic conditions. Different metal complexes have been proposed as catalysts: they include Grubbs' ruthenium complexes,[12] ruthenium-grafted hydrotalcite,[13] $RuCl_2(dmso)_4$,[14] $RhCl(PPh_3)_3$,[15] palladium on charcoal,[16] $[IrCl(cod)]_2$[17] and $CuCl_2$.[18] It is not only the carbonyl electrophilic partner 2-aminobenzaldehyde (**1a**: R^1 = R^2 = H) that can be substituted by the corresponding benzyl alcohol by this approach: ketones **2** can also be substituted by the corresponding secondary alcohols.[19] Here we report the expansion of this indirect approach to the Friedländer annulation not only with synthetic equivalents of simple 2-aminobenzaldehyde but also with more challenging systems such as 2-aminobenzophenone derivatives. The $RuCl_2(dmso)_4$[20] complex was chosen as catalyst, since it has shown excellent activity both as a hydrogen-transfer catalyst[21] (needed for the first stage of the process) and as

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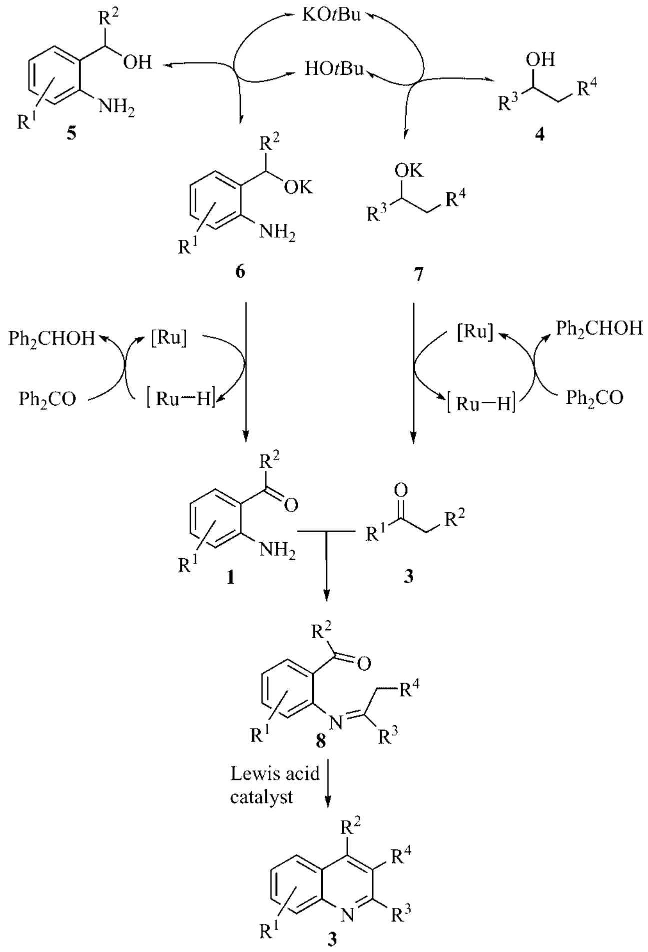
a Lewis acid[22] (needed for the annulation process with 2-aminobenzophenone derivatives), with both activities being very important for the success of the whole process.

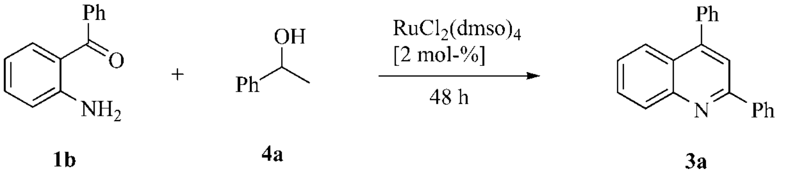
Results and Discussion

We began our study by optimizing the reaction conditions between 2-aminobenzophenone (**1b**) and 1-phenylethanol (**4a**) to give the corresponding quinoline **3a** (Table 1). The initial reaction conditions gave the expected product with a modest yield (Table 1, Entry 1), but it should be pointed out that, although the yield was not very high, this is the first 4-phenylquinoline synthesis by an indirect Friedländer approach and that the modest yield could be due to difficulty in the re-oxidation of the ruthenium hydride formed in situ (see mechanistic considerations below in Scheme 2). Under these conditions, this re-oxidation could be performed either by the reaction of ruthenium hydride formed in situ with oxygen,[23] or by the direct formation of molecular hydrogen.[24] The presence of an organic scavenger of hydrogen such as benzophenone or the addition of an extra amount of alcohol **4a** had a small influence on the result (Table 1, Entries 2 and 3), but the removal of the solvent had a great impact (Table 1, Entries 4 and 5), with the reaction giving an excellent chemical yield under solvent-free conditions.[25] It is notable that these conditions also offer several other advantages, such as, among others, ease of workup and the low amount of energy used in the heating. While a doubling of the amount of base produced a marginal increase in the yield (Table 1, Entry 6), any reduction in the amount of base or change in the nature of the hydrogen scavenger had an important detrimental effect (Table 1, Entries 7 and 8). The nature of



Scheme 2. Proposed catalytic indirect Friedländer annulation process.

Table 1. Optimization process.



Entry	Solvent	Base [mol-%]	T [°C]	Hydrogen scavenger [mol-%]	Yield[a] [%]
1	1,4-dioxane	KOH [100]	100	–	47
2	1,4-dioxane	KOH [100]	100	benzophenone [100]	57
3[b]	1,4-dioxane	KOH [100]	100	benzophenone [100]	53
4	solvent-free	KOH [100]	100	benzophenone [100]	92
5[c]	solvent-free	KOH [100]	100	benzophenone [100]	80
6	solvent-free	KOH [200]	100	benzophenone [100]	94
7	solvent-free	KOH [10]	100	benzophenone [100]	15
8	solvent-free	KOH [100]	100	dodec-1-ene [100]	76
9	solvent-free	Na_2CO_3 [100]	100	benzophenone [100]	0
10	solvent-free	K_3PO_4 [100]	100	benzophenone [100]	0
11	solvent-free	KO*t*Bu [100]	100	benzophenone [100]	99
12[c]	solvent-free	KO*t*Bu [100]	100	benzophenone [100]	94
13	solvent-free	KO*t*Bu [100]	60	benzophenone [100]	89
14[c]	solvent-free	KO*t*Bu [100]	140	benzophenone [100]	93

[a] Isolated yields after acidic-basic aqueous extraction. [b] Two equivalents of alcohol **4a** were used. [c] Yield obtained after 24 h reaction time.

the base also had an important role: the reaction failed with bases weaker than KOH, such as Na_2CO_3 or K_3PO_4, while the use of slightly stronger bases such as potassium *tert*-butoxide gave the expected product in practically quantitative yield (compare Entries 4 and 9–11 in Table 1). Under these conditions, reduction of the reaction time gave slightly poorer results (Table 1, Entry 13). We finally studied the influence of temperature, finding that lower or higher temperatures gave worse or similar results, respectively (compare Entries 11–14 in Table 1).

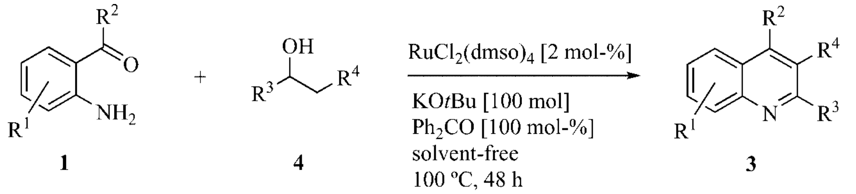
Once the best reaction conditions had been found (Table 1, Entry 11), other 2-aminophenyl ketone derivatives **1**, as well as alcohols **4**, were tested (Table 2). The reaction gave practically quantitative yields not only with 1-phenylethanol (**4a**) but also for other related 4-substituted phenyl alcohols (Table 2, Entries 1–3) independently of the electronic natures of the substituents (electron-donating group in the methyl derivative **4b** or electron-withdrawing one in the trifluoromethyl derivative **4c**). Yields were also good for the sterically hindered 1-(2-naphthyl)ethanol (**4d**) and for the acid sensitive 1-(2-furyl)ethanol (**4e**) (Table 2, Entries 4 and 5, respectively). The reaction also worked well for aliphatic alcohols such as 3,3-dimethylbutan-2-ol (**4f**; Table 2, Entry 6). Pleasingly, the reaction was regioselective in the case of heptan-2-ol, giving only one of the two possible quinoline isomers (Table 2, Entry 7), the aldol condensation taking place at the methyl position of the alcohol **4g** rather than at the methylenic one. Although the yields were lower in cases in which primary alcohols such as 2-phenylethanol (**4h**) were used, this result show the versatility of this approach (Table 2, Entry 8).

The reaction worked not only with 1-substituted ethanols but also with other alcohols with longer chains, in these cases yielding the corresponding 3-substituted quinolines (Table 2, Entries 9–11).

While the change of 2-aminobenzophenone (**1b**) for its methoxy derivative **1c** did not have any important consequence, the reaction with 2-aminoacetophenone (**1d**) produced a notable diminution of the chemical yield (compare Entries 1, 12 and 13 in Table 2). The presence of halogen atoms on the aromatic ring of the ketone **1** did not have any appreciable effect on the chemical yields (Table 2, Entries 14–19). The reaction between 2,5-diaminobenzophenone (**1f**) and the alcohol **4a** merits a separate comment, since the presence of two amino functionalities might have had a detrimental effect on the yield. However, the reaction gave the expected 6-aminoquinoline product **3t** as the only isolated product, this result indicating that the condensation of the amino group with the ketone formed in situ is essentially reversible under these reaction conditions (see Scheme 2), since it should have occurred prior to the aldol condensation.

Once we had found that the substitution of the nucleophilic carbonyl partner by the corresponding alcohol in the Friedländer annulation could be achieved in a $RuCl_2(dmso)_4$-catalysed process, we focused our attention on the

Table 2. Indirect Friedländer annulation with aminophenyl ketones **1** and alcohols **4**.

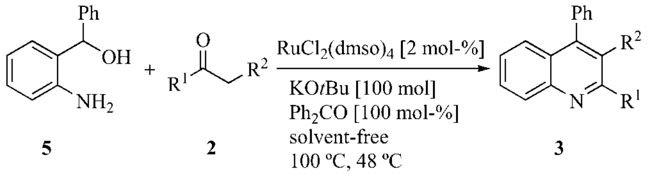


Entry	Ketone	Alcohol	Product	R^1	R^2	R^3	R^4	Yield[a] [%]
1	**1b**	**4a**	**3a**	H	Ph	Ph	H	99[b]
2	**1b**	**4b**	**3b**	H	Ph	4-MeC_6H_4	H	96[b]
3	**1b**	**4c**	**3c**	H	Ph	$4\text{-CF}_3C_6H_4$	H	99
4	**1b**	**4d**	**3d**	H	Ph	2-naphthyl	H	78
5	**1b**	**4e**	**3e**	H	Ph	2-furyl	H	85
6	**1b**	**4f**	**3f**	H	Ph	*t*Bu	H	83[b]
7	**1b**	**4g**	**3g**	H	Ph	$CH_3(CH_2)_4$	H	95
8	**1b**	**4h**	**3h**	H	Ph	H	Ph	51[b]
9	**1b**	**4i**	**3i**	H	Ph	Ph	Me	94
10	**1b**	**4j**	**3j**	H	Ph	$–(CH_2)_4–$		81[b]
11	**1b**	**4k**	**3k**	H	Ph	$–[1,2\text{-}C_6H_4(CH_2)_2]–$		88
12	**1c**	**4a**	**3l**	H	4-MeOC_6H_4	Ph	H	91
13	**1d**	**4a**	**3m**	H	Me	Ph	H	48
14	**1e**	**4a**	**3n**	6-Cl	Ph	Ph	H	98
15	**1e**	**4c**	**3o**	6-Cl	Ph	$4\text{-CF}_3C_6H_4$	H	97
16	**1e**	**4f**	**3p**	6-Cl	Ph	*t*Bu	H	79
17	**1e**	**4a**	**3q**	6-Cl	2-FC_6H_4	Ph	H	65
18	**1e**	**4a**	**3r**	6-Cl	2-ClC_6H_4	Ph	H	79
19	**1e**	**4f**	**3s**	6-Cl	2-ClC_6H_4	$4\text{-CF}_3C_6H_4$	H	75
20	**1f**	**4a**	**3t**	6-NH_2	Ph	Ph	H	65

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate). [b] Obtained yield after acidic-basic aqueous extraction.

substitution of the electrophilic carbonyl partner **1** of the reaction by the related alcohol **5** (Table 3). Treatment of the ketone **2** with the alcohol **5** in the presence of potassium *tert*-butoxide under solvent-free conditions thus gave the expected quinolines **3** with results similar to those obtained previously, indicating that the replacement of the ketone **1** by its alcohol derivative is also possible.

Table 3. Indirect Friedländer annulation with the alcohol **5** and ketones **2**.

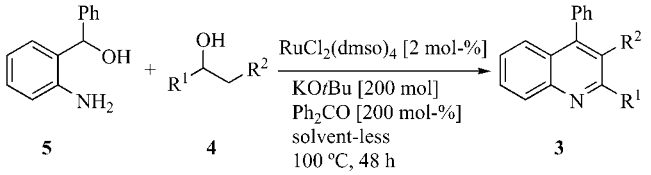


Entry	Ketone	Product	R^1	R^2	Yield[a] [%]
1	**2a**	**3a**	Ph	H	64
2	**2b**	**3b**	4-MeC_6H_4	H	73
3	**2c**	**3k**	–[1,2-$C_6H_4(CH_2)_2$]–		85[b]

[a] Isolated yields after acidic-basic aqueous extraction. [b] Obtained yield after column chromatography (silica gel: hexane/ethyl acetate).

Finally we studied the possible double replacement of both the nucleophilic and the electrophilic components in this process (Table 4). Thus, treatment of the alcohol **4** (source of the nucleophilic carbonyl partner in the classical procedure) with the amino alcohol **5** (source of the electrophilic carbonyl partner) gave results similar to those obtained previously on changing only one of the two components of the reaction. In these cases it needs to be taken in account that, although the amount of catalyst is the same as in previous cases, the real equivalents are halved, owing to the presence of two equivalents of alcohols to be oxidized. In addition, it is remarkable that the yield for the primary alcohol was lower than for secondary ones (compare Entries 1, 2 and 4 with Entry 3 in Table 4).

Table 4. Indirect Friedländer annulation with alcohols **4** and **5**.



Entry	Alcohol	Product	R^1	R^2	Yield[a] [%]
1	**4a**	**3a**	Ph	H	72
2	**4b**	**3b**	4-MeC_6H_4	H	87
3	**4h**	**3h**	H	Ph	43
4	**4j**	**3j**	–$(CH_2)_4$–		92

[a] Isolated yields after acidic-basic aqueous extraction.

Finally, the possible catalytic cycle merits a separate comment (Scheme 2). According to our previous proposed catalytic cycle for the related process,[14b] we had supposed that the necessity to use stoichiometric amounts of base is to force the formation of the corresponding potassium alkoxide **6** and/or **7**, which are the real substrates for the hydride abstraction. The ruthenium catalytic species [Ru], which is not necessarily the starting ruthenium complex, reacts with the alkoxide to yield the corresponding carbonyl compounds **1** and **3**, and a ruthenium hydride intermediate, which is re-oxidized by reaction with benzophenone. Other possible routes for ruthenium re-oxidation might also compete with the reported main pathway. The condensation of the two carbonyl compounds **1** and **3** yields the imine derivative **8**, which gives rise to the corresponding polysubstituted quinoline through a Lewis acid-catalyzed process, according to the previously mentioned literature.

Conclusions

This study represents the first example of an indirect Friedländer synthesis of 4-substituted or 4,6-disubstituted quinolines with the use of alcohols as reagents. This technique has several advantages, such as the ease of workup and product purification, the absence of solvents and strong acid catalysts, and the ease of storage of reagents. The reaction is catalyzed efficiently by $RuCl_2(dmso)_4$, giving the corresponding quinoline derivatives in good to excellent yields. The yields are practically independent either of the nature of the alcohol used (aromatic or aliphatic) or of its substitution (primary or secondary alcohols). The catalyst used is very cheap, stable and easy to handle and to prepare. The reaction is regioselective with regard to the carbonyl component formed in situ, taking place at its less substituted position.

Experimental Section

General Remarks: Full general statements have been detailed elsewhere.[26] Ketone **1c**[27] was prepared in 81 % overall yield by treatment of isatoic anhydride with *N,O*-dimethylhydroxylamine hydrochloride in aqueous ethanol to give the corresponding 2-aminobenzamide, which then was treated with 4-methoxyphenyllithium obtained in situ from butyllithium and 4-bromoanisole by literature procedures.[28] Alcohol **5**[29] was prepared in 87 % yield by standard reduction of the ketone **1b** with $NaBH_4$ in ethanol.[30] The $RuCl_2(dmso)_4$ complex was prepared in excellent yields (85–99 %) by brief heating of $RuCl_3 \cdot 3H_2O$ at reflux in dimethyl sulfoxide.[31] Other reagents were commercially available (Acros, Aldrich, Strem) and were used as received. Solvents were dried by standard procedures.[32]

General Procedure for the Indirect Friedländer Annulation: The corresponding alcohol **4** or ketone **2** (2 mmol) and potassium *tert*-butoxide (0.24 g, 2 mmol) were added to a mixture of $RuCl_2(dmso)_4$ (0.02 g, 0.02 mmol) and the corresponding 2-aminophenyl ketone or alcohol derivative (**1** or **5**, 2 mmol). The resulting mixture was heated at 100 °C with stirring for 48 h. The reaction mixture was then allowed to cool to room temperature and quenched by the successive addition of a saturated solution of NH_4Cl (10 mL) and ethyl acetate (10 mL). The mixture was filtered off through celite and extracted with acetate (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated (15 Torr) to give a residue, which was purified by column chromatography on silica gel with suitable mixtures of hexane/ethyl acetate. Alternatively (see Tables 1 to Table 4), the resulting residue was dissolved in ethyl acetate (10 mL) and extracted with hydrochloric acid (2 м, 3 × 10 mL). The resulting aqueous solution was subsequently basified with a solution of NaOH (3 м) until pH 13, producing a suspension, which was finally extracted with acetate (3 × 10 mL), and the combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated (15 Torr) to afford the pure quinoline **5**. Yields are included in Tables 1 to 4. Physical and spectroscopic data follow, together with literature references for known compounds.

2,4-Diphenylquinoline (3a):[33] Colorless solid (0.56 g, 99 %), m.p. 111–113 °C. t_r = 20.7. R_f = 0.60 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.43–7.55, 7.70–7.75, 7.80, 7.85–7.90 and 8.15–8.25 (2 × m, s and 2 × m, respectively, 9, 1, 1, 1 and 3 H, respectively, ArH) ppm. ^{13}C NMR: δ = 119.30, 125.55, 125.70, 126.30, 127.55 (2 C), 128.35, 128.55 (2 C), 128.80 (2 C), 129.30, 129.45, 129.50 (2 C), 130.10, 138.35, 139.60, 148.75, 149.10, 156.85 ppm. IR (KBr): $\tilde{\nu}$ = 3055, 1597, 1496, 1402 cm^{-1} (C=CH). MS: m/z (%) = 281 (69) [M]$^+$, 280 (100), 202 (11).

2-(4-Methylphenyl)-4-phenylquinoline (3b):[33] Colorless oil (0.57 g, 99 %), t_r = 22.7. R_f = 0.65 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 2.39 (s, 3 H, CH_3), 7.29 and 8.08 (2 × d, J = 8 and 8 Hz, 2 H each, $C_6H_4CH_3$), 7.40–7.45, 7.65–7.70, 7.75, 7.85 and 8.21 (2 × m, s and 2 × d, respectively, J = 8 and 8 Hz, 1 H each, quinoline $H^{3,5,6,7,8}$), 7.45–7.55 (m, 5 H, Ph) ppm. ^{13}C NMR: δ = 21.25, 119.10 (2 C), 125.50, 125.60, 126.05, 127.35 (2 C), 128.25, 128.45 (2 C), 129.35, 129.50 (2 C), 129.95 (2 C), 136.75, 138.40, 139.30, 148.75, 148.95, 156.70 ppm. IR (film): $\tilde{\nu}$ = 3055, 1591, 1542, 1492 cm^{-1} (C=CH). MS: m/z (%) = 295 (73) [M]$^+$, 294 (100), 202 (10).

4-Phenyl-2-(4-trifluoromethylphenyl)quinoline (3c): Colorless solid (0.68 g, 99 %), m.p. 76–78 °C. t_r = 20.1. R_f = 0.71 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.40–7.45, 7.65–7.75, 7.85 and 8.20–8.25 (2 × m, dd and m, respectively, J = 0.9 and 8.4 Hz, 6, 4, 1 and 3 H, respectively, ArH) ppm. ^{13}C NMR: δ = 124.20 (q, $^FJ_{1,2}$ = 272.2 Hz, CF_3), 125.5–125.65 (m, 3 C), 125.90, 126.75, 127.70, (2 C), 128.50, 128.55 (2 C), 129.45 (2 C), 129.70, 130.20, 130.95 (q, $^FJ_{1,3}$ = 32.9 Hz, CCF_3), 138.05, 142.75, 148.70, 149.45, 154.95 ppm. IR (KBr): $\tilde{\nu}$ = 3069, 1625, 1585, 1555 cm^{-1} (C=CH). MS: m/z (%) = 350 (14) [M + 1]$^+$, 349 (69), 348 (100), 202 (100). HRMS calcd. for $C_{22}H_{14}F_3N$: 349.1078; found: 349.1054.

2-(Naphthalen-2-yl)-4-phenylquinoline (3d):[34] Pale yellow oil (0.52 g, 78 %), t_r = 32.1. R_f = 0.67 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.45–7.60 (m, 9 H, ArH), 7.65 (s, 1 H, quinoline H^3), 7.65–7.80 and 7.90–7.95 (2 × m, 2 H each, ArH), 8.00 (d, J = 8.4 Hz, 1 H, quinoline H^5), 8.20–8.25 (m, 1 H, ArH), 8.30 (d, J = 8.4 Hz, 1 H, quinoline H^8) ppm. ^{13}C NMR: δ = 123.40, 125.35, 125.50, 125.65, 125.70, 125.90, 126.60, 127.80, 128.35, 128.40, 128.55 (2 C), 129.10, 129.55, 129.60 (2 C), 130.10, 131.25, 134.00 (2 C), 138.05, 138.65, 148.65 (2 C), 158.95 ppm. IR (film): $\tilde{\nu}$ = 3054, 1585, 1541, 1492 cm^{-1} (C=CH). MS: m/z (%) = 332 (13) [M + 1]$^+$, 331 (63), 330 (100), 328 (20), 254 (45), 164 (16).

2-(Furan-2-yl)-4-phenylquinoline (3e):[33] Yellow oil (0.56 g, 85 %), t_r = 20.1. R_f = 0.56 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 6.59 and 7.23 (2 × d, J = 1.4 and 3.4 Hz, respectively, 1 H each, OCH=C*HCH*), 7.50–7.55 and 7.62 (m and s, respectively, 6 and 1 H, respectively, Ph and OC*H*=CH), 7.25–7.45, 7.70–7.75, 7.77, 7.85 and 8.19 (2 × m, s and 2 × d, J = 8.4 and 8.4 Hz, 1 H each, quinoline $H^{3,5,6,7,8}$) ppm. ^{13}C NMR: δ = 110.15, 112.20, 117.70, 125.70, 125.80, 126.20, 128.45, 128.55 (2 C), 129.50 (2 C), 129.70, 129.75, 138.15, 144.10, 148.55, 148.65, 149.10, 153.75 ppm. IR (film): $\tilde{\nu}$ = 3066, 1592, 1545 cm^{-1} (C=CH). MS: m/z (%) = 272 (20) [M + 1]$^+$, 271 (100), 270 (23), 243 (16), 242 (15), 241 (24).

2-(*tert*-Butyl)-4-phenylquinoline (3f):[33] White solid (0.43 g, 83 %), m.p. 79–80 °C. t_r = 16.8. R_f = 0.79 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 1.49 [s, 9 H, $C(CH_3)_3$], 7.35–7.40, 7.60–7.65, 7.83 and 8.12 (2 × m and 2 × d, respectively, J = 8.4 and 8.4 Hz, 1 H each, quinoline $H^{5,6,7,8}$), 7.40–7.50 (m, 6 H, Ph and quinoline H^3) ppm. ^{13}C NMR: δ = 30.15 (3 C), 38.10, 118.40 (2 C), 124.95, 125.30, 125.60, 128.10, 128.45, 128.80, 129.55 (2 C), 129.75, 138.80, 147.90, 148.10, 168.70 ppm. IR (film): $\tilde{\nu}$ = 3062, 1596, 1571, 1554 cm^{-1} (C=CH). MS: m/z (%) = 261 (36) [M]$^+$, 260 (29), 247 (20), 246 (100), 219 (47), 205 (14), 204 (20).

2-Pentyl-4-phenylquinoline (3g): White oil (0.52 g, 95 %), t_r = 17.6. R_f = 0.56 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 0.85–0.95, 1.35–1.45, 1.80–1.90 and 2.95–3.00 [4 × m, 3, 4, 2 and 2 H, respectively, $(CH_2)_4CH_3$], 7.22 (s, 1 H, quinoline H^3), 7.45–7.50 (m, 5 H, Ph), 7.35–7.45, 7.60–7.65, 7.84 and 8.12 (2 × m and 2 × d, respectively, J = 8.3 and 8.3 Hz, 1 H each, quinoline $H^{5,6,7,8}$) ppm. ^{13}C NMR: δ = 13.90, 22.45, 29.65, 31.70, 39.20, 121.40, 125.10, 125.45, 125.55, 128.10, 128.35 (2 C), 129.00, 129.10, 129.35 (2 C), 138.15, 148.30, 148.35, 162.45 ppm. IR (film): $\tilde{\nu}$ = 3063, 1584, 1549 cm^{-1} (C=CH). MS: m/z (%) = 275 (2) [M]$^+$, 246 (12), 232 (20), 220 (18), 219 (100). HRMS calcd. for $C_{20}H_{21}N$: 275.1674; found: 275.1675.

3,4-Diphenylquinoline (3h):[35] Pale yellow solid (0.29 g, 51 %), t_r = 19.9. R_f = 0.45 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.15–7.25, 7.30–7.35, 7.45–7.50 and 7.70–7.75 (4 m, 7, 3, 1 and 2 H, respectively, ArH), 8.19 (d, J = 8.2 Hz, 1 H, quinoline H^8), 9.00 (s, 1 H, quinoline H^2) ppm. ^{13}C NMR: δ = 126.55, 126.85, 127.00 (2 C), 127.20, 127.70, 128.05, 128.10 (2 C), 129.05, 129.45, 130.10 (2 C), 130.50 (2 C), 133.10, 136.25, 138.10, 145.45, 147.50, 151.75 ppm. IR (film): $\tilde{\nu}$ = 3063, 1560, 1501 cm^{-1} (C=CH). MS: m/z (%) = 282 (21) [M + 1]$^+$, 281 (100), 280 (63), 278 (12), 266 (11), 252 (17), 139 (11).

3-Methyl-2,4-diphenylquinoline (3i): Pale yellow solid (0.55 g, 94 %), m.p. 131–133 °C. t_r = 22.4. R_f = 0.57 (hexane/ethyl acetate 4/1). ^{1}H NMR: δ = 2.59 (s, 3 H, CH_3), 7.75 and 7.80–8.10 (d and m, respectively, J = 6.9 Hz, 2 and 11 H, respectively, 2 × Ph and quinoline $H^{5,6,7}$), 8.62 (d, J = 8.3 Hz, 1 H, quinoline H^8) ppm. ^{13}C NMR: δ = 18.50, 125.90, 126.15, 126.65, 127.00, 127.75, 128.00, 128.25 (2 C), 128.45, 128.55 (2 C), 128.85 (2 C), 129.25 (2 C), 129.40, 137.65, 141.50, 146.20, 147.70, 160.75 ppm. IR (film): $\tilde{\nu}$ = 3058, 1617, 1575, 1554 cm^{-1} (C=CH). MS: m/z (%) = 295 (40) [M]$^+$, 294 (100). HRMS calcd. for $C_{22}H_{17}N$: 295.1361; found: 295.1357.

9-Phenyl-1,2,3,4-tetrahydroacridine (3j):[36] Pale yellow solid (0.48 g, 92 %), m.p. 136–138 °C. t_r = 17.9. R_f = 0.69 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 1.75–1.85, 1.95–2.00, 2.60 and 3.18 [2 × m and 2 × t, respectively, J = 6.7 and 7 Hz, respectively, 2 H each, $(CH_2)_4$], 7.20–7.30, 7.40–7.60 and 7.98 (2 × m and d, respectively, J = 8.0 Hz, 4, 4 and 1 H, respectively, ArH) ppm. ^{13}C NMR: δ = 22.85, 23.00, 28.00, 34.20, 125.30, 125.75, 126.60, 127.65, 128.25, 128.30, 128.55 (2 C), 129.05 (2 C), 137.10 (2 C), 146.25, 146.40, 159.00 ppm. IR (film): $\tilde{\nu}$ = 3060, 1571, 1495 cm^{-1} (C=CH). MS: m/z (%) = 259 (100) [M]$^+$, 230 (12), 183 (10).

7-Phenyl-5,6-dihydrobenzo[*c*]acridine (3k):[37] White solid (0.54 g, 88 %), m.p. 149–151 °C. t_r = 28.2. R_f = 0.67 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 2.75–2.85 (m, 4 H, CH_2CH_2), 7.15–7.30, 7.35–7.50 and 7.55–7.60 (3 m, 5, 5 and 1 H, respectively, ArH), 8.16 and 8.62 (2 × d, J = 8.4 and 7.6 Hz, respectively, 1 H each, quinoline $H^{5,8}$) ppm. ^{13}C NMR: δ = 26.40, 28.15, 125.80, 125.90, 126.30, 127.15, 127.60, 127.80, 127.95 (2 C), 128.35, 128.45 (2 C), 129.40 (2 C), 129.55 (2 C), 135.00, 136.85, 139.15, 145.20, 147.15, 153.00 ppm. IR (film): $\tilde{\nu}$ = 3062, 1583, 1551 cm^{-1} (C=CH). MS: *m*/*z* (%) = 308 (23) [M + 1]$^+$, 307 (100), 306 (89), 305 (14), 304 (26).

4-(4-Methoxyphenyl)-2-phenylquinoline (3l):[38] Pale yellow oil (0.57 g, 91%), t_r = 29.0. R_f = 0.47 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 3.85 (s, 3 H, OCH$_3$), 7.05, 7.40–7.50 and 7.65–7.70 (d and 2 × m, respectively, *J* = 9.5 Hz, 2, 6 and 1 H, respectively, Ph and C$_6$H$_4$O), 7.77, 7.92, 8.15–8.20 and 8.22 (s, d, m and d, respectively, *J* = 8.4 and 8.4 Hz, 1, 1, 2 and 1 H, respectively, quinoline H^{3,5,6,7,8}) ppm. ^{13}C NMR: δ = 55.35, 114.00 (2 C), 119.25, 125.60, 125.90, 126.15, 127.50 (2 C), 128.75 (2 C), 129.20, 129.35, 130.05, 130.60, 130.75 (2 C), 139.70, 148.80, 148.85, 156.85, 159.80 ppm. IR (film): $\tilde{\nu}$ = 3060, 1613, 1553, 1508 (C=CH), 2836 cm^{-1} (OCH$_3$). MS: *m*/*z* (%) = 312 (22) [M + 1]$^+$, 311 (100), 310 (84), 280 (28), 267 (29).

4-Methyl-2-phenylquinoline (3m):[33] Pale yellow oil (0.21 g, 48%), t_r = 18.3. R_f = 0.57 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 2.76 (s, 3 H, CH$_3$), 7.45–7.55, 7.70–7.75, 7.99 and 8.15–8.20 (2 × m, d and m, respectively, *J* = 8.4 Hz, 4, 2, 1 and 3 H, respectively, ArH) ppm. ^{13}C NMR: δ = 19.00, 119.75, 123.60, 126.00, 127.25, 127.50 (2 C), 128.75 (2 C), 129.15, 129.30, 130.30, 139.80, 144.75, 148.10, 157.05 ppm. IR (film): $\tilde{\nu}$ = 3060, 1602, 1547, 1514, 1492 cm^{-1} (C=CH). MS: *m*/*z* (%) = 220 (17) [M + 1]$^+$, 219 (100), 218 (43), 217 (23), 205 (12), 204 (72), 108 (13).

6-Chloro-2,4-diphenylquinoline (3n):[33] Colorless needles (0.62 g, 98%), m.p. 130–132 °C. t_r = 23.1. R_f = 0.61 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.40–7.55 and 7.60–7.65 (2 × m, 8 and 1 H, respectively, ArH), 7.81 (s, 1 H, quinoline H^3), 7.84 (d, *J* = 2.3 Hz, 1 H, ArH), 8.13 (s, 1 H, quinoline H^5), 8.15–8.20 (m, 2 H, ArH) ppm. ^{13}C NMR: δ = 119.95, 124.40, 126.40, 127.45 (2 C), 128.65, 128.75 (2 C), 128.85 (2 C), 129.40 (2 C), 129.50, 130.35, 131.70, 132.15, 137.70, 139.15, 147.15, 148.35, 157.00 ppm. IR (film): $\tilde{\nu}$ = 3063, 1593, 1549 cm^{-1} (C=CH). MS: *m*/*z* (%) = 317 (32) [M + 2]$^+$, 316 (50), 315 (95), 314 (100), 280 (32), 278 (15), 201 (12), 139 (18), 139 (20).

6-Chloro-4-phenyl-2-(4-trifluoromethylphenyl)quinoline (3o): Pale yellow solid (0.74 g, 97%), m.p. 141–143 °C. t_r = 24.8. R_f = 0.70 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.45–7.65, 7.70–7.80, 7.85, 8.10 and 8.25 (2 × m, s and 2 × d, respectively, *J* = 9.0 and 8.3 Hz, respectively, 6, 3, 1, 1 and 2 H, respectively, ArH) ppm. ^{13}C NMR: δ = 119.65, 124.10 (q, $^{F}J_{1,2}$ = 272.2 Hz, CF$_3$), 124.45, 125.60–125.75 (m, 3 C), 126.65, 127.70 (2 C), 128.80 (2 C), 129.35 (2 C), 130.65, 131.20 (q, $^{F}J_{1,3}$ = 32.9 Hz, *C*CF$_3$), 131.75, 132.75, 137.40, 142.30, 147.10, 148.75, 155.20 ppm. IR (film): $\tilde{\nu}$ = 3069, 1596, 1490 cm^{-1} (C=CH). MS: *m*/*z* (%) = 385 (33) [M$^+$ + 2], 384 (50), 383 (100), 382 (94), 349 (10), 348 (43), 202 (10), 201 (11), 176 (11), 174 (14), 163 (13), 139 (11). HRMS calcd. for C$_{22}$H$_{13}$ClF$_3$N: 383.0689; found: 383.0685.

2-(*tert*-Butyl)-6-chloro-4-phenylquinoline (3p):[33] Pale yellow oil (0.47 g, 79%), t_r = 17.9. R_f = 0.75 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 1.48 [s, 9 H, C(CH$_3$)$_3$], 7.45–7.60 (m, 7 H, ArH), 7.80 and 8.05 (2 × d, *J* = 2.3 and 8.9 Hz, respectively, 1 H each, quinoline H^{5,8}) ppm. ^{13}C NMR: δ = 30.10 (3 C), 38.20, 119.20, 124.20, 125.75, 128.45, 128.70 (2 C), 129.45 (2 C), 29.70, 131.45, 131.50, 138.15, 146.35, 147.45, 169.15 ppm. IR (film): $\tilde{\nu}$ = 3066, 1594, 1549 cm^{-1} (C=CH). MS: *m*/*z* (%) = 297 (11) [M$^+$ + 2], 296 (14), 295 (33), 294 (25), 282 (33), 281 (20), 280 (100), 255 (18), 254 (10), 253 (53), 204 (11), 203 (15), 122 (10).

6-Chloro-4-(2-fluorophenyl)-2-phenylquinoline (3q): White solid (0.43 g, 65%), m.p. 128–130 °C. t_r = 24.9. R_f = 0.65 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.20–7.30, 7.40–7.50 and 7.60–7.65 (3 m, 2, 5 and 2 H, respectively, ArH), 7.84 (s, 1 H, quinoline H^3), 8.15–8.20 (m, 3 H, ArH) ppm. ^{13}C NMR: δ = 116.20 (d, $^{F}J_{1,3}$ = 21.5 Hz), 120.85, 124.35 (d, $^{F}J_{1,3}$ = 18.8 Hz), 124.50, 125.05 (d, $^{F}J_{1,4}$ = 16.2 Hz), 126.55, 127.45 (2 C), 128.80 (2 C), 129.55, 130.50, 130.80 (d, $^{F}J_{1,5}$ = 8.1 Hz), 131.55, 131.60 (d, $^{F}J_{1,4}$ = 14.8 Hz), 132.35, 138.95, 142.45, 146.95, 156.95, 159.55 (d, $^{F}J_{1,2}$ = 249.3 Hz) ppm. IR (film): $\tilde{\nu}$ = 3049, 1615, 1596, 1542 cm^{-1} (C=CH). MS: *m*/*z* (%) = 335 (34) [M + 2]$^+$, 334 (49), 333 (100), 332 (92), 298 (33), 296 (13), 149 (15), 148 (13). HRMS calcd. for C$_{21}$H$_{13}$ClFN: 333.0721; found: 333.0731.

6-Chloro-4-(2-chlorophenyl)-2-phenylquinoline (3r): White needles (0.55 g, 79%), m.p. 110–112 °C. t_r = 28.2. R_f = 0.62 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.35–7.65 (m, 9 H, ArH), 7.81 (s, 1 H, quinoline H^5), 8.15–8.20 (m, 3 H, ArH) ppm. ^{13}C NMR: δ = 120.50, 124.30, 12.45, 126.90, 127.50 (2 C), 128.83 (2 C), 129.60, 130.00, 130.55, 131.25, 131.65, 132.25, 133.20, 136.25, 138.95, 145.65, 146.85, 156.90 ppm. IR (film): $\tilde{\nu}$ = 3067, 1606, 1592, 1546 cm^{-1} (C=CH). MS: *m*/*z* (%) = 353 (11) [M + 4]$^+$, 352 (20), 351 (65), 350 (61), 349 (100), 348 (63), 316 (18), 315 (14), 314 (56), 278 (20), 277 (15), 201 (11), 139 (30), 125 (13). HRMS calcd. for C$_{21}$H$_{13}$Cl$_2$N: 349.0425; found: 349.0421.

6-Chloro-4-(2-chlorophenyl)-2-(4-trifluoromethylphenyl)quinoline (3s): White solid (0.62 g, 75%), m.p. 163–165 °C. t_r = 26.1. R_f = 0.61 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 7.35–7.50, 7.60–7.70, 7.78, 7.84, 8.18 and 8.30 (2 × m, d, s and 2 × d, respectively, *J* = 8.2, 8.9 and 8 Hz, respectively, 4, 2, 2, 1, 1 and 2 H, respectively, ArH) ppm. ^{13}C NMR: δ = 120.35, 124.10 (q, $^{F}J_{1,2}$ = 272.2 Hz, CF$_3$), 124.40, 125.75–125.85 (m, 2 C), 126.75, 127.05, 127.80 (2 C), 131.40 (q, $^{F}J_{1,3}$ = 32.3 Hz, *C*CF$_3$), 130.15, 130.30, 130.95, 131.25, 131.80, 133.00, 133.20, 136.00, 142.30, 146.15, 146.90, 155.30 ppm. IR (film): $\tilde{\nu}$ = 3053, 1619, 1610, 1583 cm^{-1} (C=CH). MS: *m*/*z* (%) = 421 (11) [M + 4]$^+$, 420 (20), 419 (66), 418 (57), 417 (100), 416 (54), 384 (23), 383 (17), 382 (66), 346 (11), 201 (10), 173 (10). HRMS calcd. for C$_{22}$H$_{12}$Cl$_2$F$_3$N: 417.0299; found: 417.0310.

6-Amino-2,4-diphenylquinoline (3t): Orange oil (0.38 g, 65%), t_r = 32.2. R_f = 0.17 (hexane/ethyl acetate 4:1). ^{1}H NMR: δ = 3.90 (s, 2 H, NH$_2$), 6.95, 7.15, 7.25, 7.40–7.55, 7.70, 8.05 and 8.10–8.15 (d, dd, s, m, s, d and m, respectively, *J* = 2.6, 2.6, 9 and 9 Hz, respectively, 1, 1, 8, 1, 1 and 2 H, respectively, ArH) ppm. ^{13}C NMR: δ = 105.65, 119.60, 121.40, 127.15 (2 C), 128.05, 128.50 (2 C), 128.65, 128.70 (2 C), 129.40 (2 C), 131.30, 138.95, 139.90 (2 C), 143.85, 144.65, 146.65, 153.40 ppm. IR (film): $\tilde{\nu}$ = 3386, 3217 (NH$_2$), 3063, 1624, 1592, 1551 cm^{-1} (C=CH). MS: *m*/*z* (%) = 297 (23) [M + 1]$^+$, 296 (100), 295 (52). HRMS calcd. for C$_{21}$H$_{16}$N$_2$: 296.1313; found: 296.1310.

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