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PAPER

Ruthenium-catalysed synthesis of 2- and 3-substituted quinolines from anilines and 1,3-diols†

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A straightforward synthesis of substituted quinolines is described by cyclocondensation of anilines with 1,3-diols. The reaction proceeds in mesitylene solution with catalytic amounts of $RuCl_3 \cdot xH_2O$, PBu_3 and $MgBr_2 \cdot OEt_2$. The transformation does not require any stoichiometric additives and only produces water and dihydrogen as byproducts. Anilines containing methyl, methoxy and chloro substituents as well as naphthylamines were shown to participate in the heterocyclisation. In the 1,3-diol a substituent was allowed in the 1- or the 2-position giving rise to 2- and 3-substituted quinolines, respectively. The best results were obtained with 2-alkyl substituted 1,3-diols to afford 3-alkylquinolines. The mechanism is believed to involve dehydrogenation of the 1,3-diol to the 3-hydroxyaldehyde which eliminates water to the corresponding α,β-unsaturated aldehyde. The latter then reacts with anilines in a similar fashion as observed in the Doebner–von Miller quinoline synthesis.

Introduction

Quinolines are one of the major classes of heterocycles and the quinoline ring system is found in many natural products.[1] Substituted quinolines are widely used in medicinal chemistry particularly as antimalaria,[2] antituberculosis,[3] anticancer[4] and antivial[5] agents. Quinoline derivatives also find significant applications as agrochemicals[6] and dyes.[7] The synthesis of quinolines has gained broad attention for more than a century and numerous approaches have been developed. The classical methods include the Combes synthesis from anilines and 1,3-diketones, the Skraup (or Doebner–von Miller) synthesis from anilines and glycerol (or α,β-unsaturated aldehydes/ketones), and the Friedländer synthesis from *ortho*-acylanilines and α-methylene aldehydes/ketones.[8] More recently, aza-Diels–Alder reactions between *N*-arylaldimines and dienophiles, three component reactions between anilines, aldehydes and α-methylene aldehydes/ketones, as well as various metal-catalysed cyclisations with *ortho*-substituted anilines have found many applications for assembling the quinoline skeleton.[9] The development of new quinoline syntheses continue to gain considerable interest and lately focus has shifted towards more environmentally friendly processes using transition metal catalysis and alcohol substrates.[10] Modified Friedländer syntheses have been developed with *o*-aminobenzyl alcohol which has been coupled with ketones or secondary alcohols in the presence of a range of metal catalysts.[11] Amine exchange reactions have been employed between aniline

and 3-aminoalcohols catalysed by $RuCl_3 \cdot xH_2O/PPh_3$ and stoichiometric amounts of $SnCl_2 \cdot 2H_2O$.[12,13] Cyclocondensation of aniline with propane-1,3-diol in refluxing diglyme with catalytic amounts of $RuCl_3 \cdot xH_2O/PBu_3$ also affords the quinoline ring system.[14] The same reaction can be achieved with 1-naphthylamine and catalytic amounts of $IrCl_3 \cdot 3H_2O/BINAP$ under an oxygen atmosphere in refluxing mesitylene.[15] In the latter two cases, however, a significant excess of the arylamine is employed for the heterocyclisation.
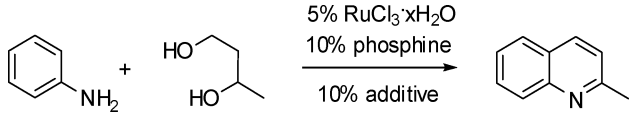
We have previously employed $[Cp*IrCl_2]_2$ as (pre)catalyst for the synthesis of piperazines from (di)amines and 1,2-diols.[16] In addition, C-3 alkylation of oxindole with alcohols has been achieved under neat conditions with $RuCl_3 \cdot xH_2O/PPh_3$ as the catalyst.[17] Very recently, we employed both the iridium and the ruthenium catalyst for the synthesis of indoles from anilines and 1,2-diols.[18] We speculated that the two catalyst systems would mediate a similar synthesis of quinolines from anilines and 1,3-diols. Herein, we describe our studies on the ruthenium-catalysed cyclocondensation of anilines with various 1,3-diols. In a single step, this transformation gives rise to 2- or 3-substituted quinolines with water and dihydrogen as the only byproducts.

Results and discussion

The initial experiments were carried out with equimolar amounts of aniline and butane-1,3-diol in the absence of a solvent. The reactions were performed at 170 °C in a closed vial with either $[Cp*IrCl_2]_2$ or $RuCl_3 \cdot xH_2O/PBu_3$ as the catalyst. However, these conditions led to almost exclusive *N*-alkylation of aniline, *i.e.* formation of *N*-ethylaniline as the major product and some *N*-butylaniline and double *N*-alkylated compounds as minor products. The formation of these alkylated anilines is due to

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Table 1 Synthesis of 2-methylquinoline from aniline and butane-1,3-diol[a]

Entry	Phosphine	Additive	Yield[b]
1	PBu$_3$	—	11%
2	PBu$_3$	HCl	13%
3	PBu$_3$	MgCl$_2$	18%
4	PBu$_3$	MgBr$_2$	15%
5	PBu$_3$	MgBr$_2$·OEt$_2$	24%
6	PBu$_3$	CsBr	17%
7	PBu$_3$	SiO$_2$	19%
8	PBu$_3$	MgBr$_2$·OEt$_2$[c]	14%
9	PBu$_3$	MgBr$_2$·OEt$_2$[d]	30%[e]
10	PBu$_3$	MgBr$_2$·OEt$_2$[f]	22%
11	POct$_3$	MgBr$_2$·OEt$_2$[d]	14%
12	dppp[g]	MgBr$_2$·OEt$_2$[d]	17%
13	dppb[g]	MgBr$_2$·OEt$_2$[d]	16%
14	xantphos[g]	MgBr$_2$·OEt$_2$[d]	11%

[a] Performed with aniline (182 μL, 2 mmol), butane-1,3-diol (180 μL, 2 mmol), RuCl$_3$·xH$_2$O (26 mg, 0.1 mmol), phosphine (0.2 mmol) and additive (0.2 mmol) in mesitylene (0.5 mL) at reflux for 16 h. [b] Isolated yield. [c] With 1% of additive. [d] With 5% of additive. [e] 4-methylquinoline was also isolated in 4% yield. [f] With 25% of additive. [g] With 5% of phosphine.

degradation of butane-1,3-diol by a retro-aldol reaction or elimination of water after the initial dehydrogenation with the metal catalyst. The conditions were therefore changed and it was necessary to use both an open system and a solvent in order to obtain the quinoline product. With 5% of RuCl$_3$·xH$_2$O and 10% of PBu$_3$ as catalyst aniline and butane-1,3-diol were converted into 2-methylquinoline in 11% isolated yield in refluxing mesitylene (Table 1, entry 1). A slightly lower yield was obtained in refluxing diglyme and the N-alkylated anilines were still formed as major byproducts. It was believed that the electrophilic ring-closure to form the new C–C bond was the most difficult step. In line with our previous work on indoles[18] several Brønsted and Lewis acids were therefore investigated as co-catalysts for the cyclocondensation. Concentrated HCl gave essentially the same outcome as in the absence of the acid (entry 2) while other protic acids such as H$_2$SO$_4$, MsOH and NaHCO$_3$ gave lower yields (results not shown). Magnesium salts, on the other hand, gave better yields of 2-methylquinoline (entries 3–5) while a number of other Lewis acids (AlCl$_3$, InCl$_3$, TiCl$_4$, ZnBr$_2$, BF$_3$·OEt$_2$, Zn(OTf)$_2$, Sc(OTf)$_3$ and TMSOTf) failed to improve the yield (results not shown). Notably, CsBr and silica gel gave a slightly better yield compared to the absence of an additive (entry 6 and 7). The best result was obtained with MgBr$_2$·OEt$_2$ and upon reinvestigation it was found that 5% of the additive improved the isolated yield to 30% (entries 8–10). A number of phosphine ligands were investigated instead of PBu$_3$, but without improving the outcome (entries 11–14). Several common phosphines such as PPh$_3$, PtBu$_3$, PCy$_3$, P(o-tol)$_3$, dppe and BINAP gave even lower yields (results not shown).

With these results RuCl$_3$·xH$_2$O/PBu$_3$ and MgBr$_2$·OEt$_2$ appear to be the best catalyst system for the heterocyclisation. With p-methoxyaniline and butane-1,3-diol as the substrates in equimolar amounts the isolated yield of 6-methoxy-2-methylquinoline was 45%. When the ratio between RuCl$_3$·xH$_2$O and PBu$_3$ was changed from 1:2 to either 1:1 or 1:3 this yield decreased to

about 36%. The catalytically active species is believed to be a ruthenium(II) complex which is generated in situ. However, treating p-methoxyaniline, butane-1,3-diol and PBu$_3$ with Ru(COD)Cl$_2$, [Ru(p-cymene)Cl$_2$]$_2$, or Ru(PPh$_3$)$_3$Cl$_2$ only gave 18%, 24% and 32% yield, respectively. In the absence of the phosphine ligand none of the quinoline was formed in these three cases and the same was observed in the presence of [Cp*IrCl$_2$]$_2$ or Shvo's complex [Ph$_4$C$_5$O(CO)$_2$RuH]$_2$.[19] Although water is released in the reaction, molecular sieves had no effect on the yield of the cyclocondensation. These results confirm that RuCl$_3$·xH$_2$O, PBu$_3$ and MgBr$_2$·OEt$_2$ is the optimum ruthenium catalyst system for the quinoline synthesis from anilines and 1,3-diols.

With these results in hand the substrate scope could now be investigated with other anilines and diols (Table 2). These experiments were performed with an aniline:diol ratio of 1:1.2. With this ratio the reaction between p-methoxyaniline and 2-methylpropane-1,3-diol afforded 6-methoxy-3-methylquinoline in 60% yield (entry 11) while the yield was 54% with equimolar amounts of the reactants and only 36% with two equivalents of the aniline. Both the aniline and the diol had a significant impact on the yield in the heterocyclisation. Anilines with a methyl or a methoxy substituent in the para position (entries 8–13) gave 10–20% higher yield than the unsubstituted substrate (entries 1–6). A chloro substituent is tolerated in the aniline (entry 7) and affords almost the same yield as the parent molecule (entry 4). A small amount (~3%) of the dechlorinated quinoline was observed as a byproduct in the experiment with p-chloroaniline. With p-bromoaniline, however, dehalogenation was a significant side reaction leading to a 2:1 mixture of the 6-bromo-3-methylquinoline and 3-methylquinoline (results not shown). m-Methylaniline gave an inseparable 6:1 mixture of 3,7- and 3,5-dimethylquinoline with 2-methylpropane-1,3-diol (entry 14). The preferential cyclisation para to the electron-donating methyl group is also observed in the classical quinoline syntheses from substituted anilines.[8b,c] Ortho-substituted anilines reacted slower and gave slightly lower yields than the corresponding para-substituted anilines (entry 15 and 16). The two naphthylamines worked well in the cyclocondensation to produce the corresponding benzoquinolines (entry 17 and 18).

The substituents on the diol also played a major role for the success of the heterocyclisation. Only propane-1,3-diol or 1,3-diols with a single substituent (R or R′) were tolerated in the reaction. 1,3-Diols with two substituents, i.e. 1,2-disubstituted or 1,3-disubstituted diols, gave less than 10% of the corresponding quinoline. Pentane-2,4-diol, for example, underwent a retro aldol condensation under the reaction conditions and afforded N-isopropyl- and N-ethylaniline as the major products. In general, 1,3-diols with a single substituent in position 1 gave higher yields than propane-1,3-diol. Although, two regioisomers are possible with 1-substituted diols the reactions gave almost exclusively the 2-substituted quinolines (entries 2, 3 and 10). The highest yield in the cyclocondensation, however, were obtained with 2-alkyl substituted diols (entries 4, 5, 7, 8, 11 and 12) while 2-phenylpropane-1,3-diol gave a slightly lower yield (entry 6 and 13). In this way, the condensation of anilines and diols is a particular effective procedure for synthesis of 3-substituted quinolines, which are often difficult to prepare by other methods in a single step.[8c]

The mechanism of the transformation was studied briefly with aniline and commercially available 4-hydroxybutan-2-one. The reaction is believed to proceed by initial dehydrogenation

4-methylquinoline was formed. Since the 4-substituted quinoline is the opposite regioisomer compared to the product in Table 1, the condensation from 4-hydroxybutan-2-one and butane-1,3-diol are clearly not following the same pathway.

If a 1:1 mixture of nonane-1,3-diol and 4-hydroxybutan-2-one are condensed with aniline and the ruthenium catalyst, the former is converted into 2-n-hexylquinoline as in Table 2, entry 3 while the latter again affords 4-methylquinoline. In all these experiments 4-hydroxybutan-2-one is believed to react with aniline by elimination of water followed by a Michael addition to produce 4-anilinobutan-2-one and subsequently 4-methylquinoline. It is known that 4-methoxybutan-2-one reacts with aniline hydrochloride to produce 4-methylquinoline[20] and the reaction presumably occurs by elimination of methanol followed by a Michael addition.[21] Since the elimination of water and the following Michael addition are very facile reactions, the present condensation may proceed by initial dehydrogenation of the diol to the 3-hydroxyaldehyde (Scheme 2). It has been shown that certain ruthenium catalysts will selectively dehydrogenate a primary alcohol over a secondary alcohol.[22] The generated 3-hydroxyaldehyde will then eliminate water, undergo a Michael addition followed by electrophilic cyclisation.[23] The latter part involves the same steps as in the Doebner–von Miller quinoline synthesis[8b,24] and the regioselectivity with unsymmetric diols are then determined in the initial dehydrogenation reaction.
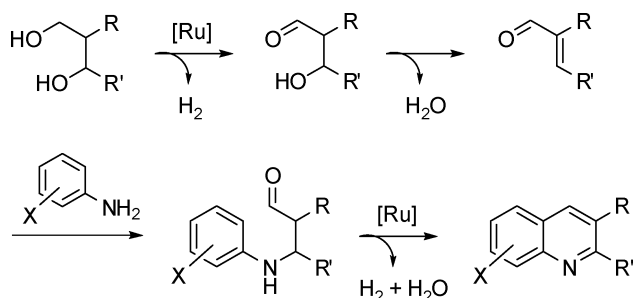
Scheme 2 Proposed mechanism for quinoline formation from anilines and 1,3-diols.

Conclusion

In summary, we have explored the one-step synthesis of quinolines from anilines and 1,3-diols with $RuCl_3 \cdot xH_2O/PBu_3$ as the catalyst. The reaction does not require any stoichiometric additives and only produces water and dihydrogen as byproducts. Increased yields are obtained when a catalytic amount of $MgBr_2 \cdot OEt_2$ is added and the transformation gives easy access to 2- and in particular 3-substituted quinolines from simple starting materials.

Experimental

Reactions were monitored by GC on a Shimadzu GC2010 instrument equipped with an Equity™ 1 column (15 m × 0.1 mm, 0.1 µm film). Melting points are uncorrected. Solvents used for chromatography were of HPLC grade. Thin layer chromatography was performed on aluminium plates coated with silica gel 60. Visualisation was done by UV or by dipping in a solution of $KMnO_4$ (1%), K_2CO_3 (6.7%) and NaOH (0.08%) in H_2O followed by heating with a heatgun. Flash chromatography was performed with silica gel 60 (35–70 µm). NMR spectra were recorded on a

Varian Mercury 300 instrument. Chemical shifts were measured relative to the signals of residual $CHCl_3$ (δ_H 7.26 ppm) and $CDCl_3$ (δ_C 77.16 ppm). Mass spectrometry was performed by direct inlet on a Shimadzu GCMS-QP5000 instrument. High resolution mass spectra were recorded at the Department of Physics and Chemistry, University of Southern Denmark.

General procedure for ruthenium-catalysed preparation of quinolines

A stirred solution of $RuCl_3 \cdot xH_2O$ (26 mg, 0.10 mmol), $MgBr_2 \cdot OEt_2$ (26 mg, 0.10 mmol), PBu_3 (50 µL, 0.20 mmol), aniline (2.0 mmol) and diol (2.4 mmol) in anhydrous mesitylene (0.50 mL) was heated to reflux under an argon atmosphere for 16 h. The reaction mixture was cooled to room temperature and purified directly by flash column chromatography (toluene–EtOAc) on silica gel pretreated with 0.1% of Et_3N in toluene.

2-n-Butyl-1,3-propanediol

Prepared from diethyl butylmalonate in 88% yield by reduction with $LiAlH_4$.[25] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (dd, J = 3.8, 10.7 Hz, 2H), 3.66 (dd, J = 7.6, 10.6 Hz, 2H), 2.04 (br s, 2 OH), 1.84–1.71 (m, 1H), 1.36–1.19 (m, 6H), 0.90 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 66.8, 42.1, 29.5, 27.5, 23.1, 14.1. MS: m/z 96 [M−2H$_2$O]. ^{1}H NMR data are in accordance with literature values.[25]

Quinoline

R_f 0.22 (toluene–EtOAc, 85:15). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.91 (d, J = 4.2 Hz, 1H), 8.13 (t, J = 8.4 Hz, 2H), 7.80 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 8.2 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.38 (dd, J = 4.2, 8.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.5, 148.4, 136.1, 129.5, 129.5, 128.4, 127.9, 126.6, 121.2. MS: m/z 129 [M]. NMR data are identical to those from a commercial sample.

2-Methylquinoline

R_f 0.26 (toluene–EtOAc, 85:15). bp 109–111 °C/8 mmHg (lit.[26] 118 °C/10 mmHg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (d, J = 8.5 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.84–7.74 (m, 2H), 7.55 (t, J = 8.1 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 2.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.7, 147.6, 135.8, 129.1, 128.4, 127.3, 126.2, 125.4, 121.7, 25.1. MS: m/z 143 [M]. NMR data are in accordance with literature values.[1h]

2-n-Hexylquinoline

R_f 0.54 (toluene–EtOAc, 85:15). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10–8.08 (m, 1H), 8.07–8.05 (m, 1H), 7.78 (dd, J = 1.3, 8.0 Hz, 1H), 7.69 (ddd, J = 1.4, 6.9, 8.4 Hz, 1H), 7.49 (ddd, J = 1.1, 7.0, 8.1 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 3.02–2.95 (m, 2H), 1.87–1.75 (m, 2H), 1.48–1.24 (m, 6H), 0.92–0.84 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.2, 147.7, 136.4, 129.5, 128.8, 127.6, 126.8, 125.8, 121.5, 39.4, 31.9, 30.2, 29.4, 22.7, 14.2. MS: m/z 213 [M]. NMR data are in accordance with literature values.[27]

3-Methylquinoline

R_f 0.24 (toluene–EtOAc, 85:15). bp 105–106 °C/4 mmHg. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.06 (d, J = 8.4 Hz, 1H),

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7.89 (s, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 152.4, 146.5, 134.7, 130.5, 129.2, 128.4, 128.1, 127.1, 126.5, 18.7. MS: m/z 143 [M]. ^{13}C NMR data are in accordance with literature values.[28]

3-*n*-Butylquinoline

R_f 0.34 (toluene–EtOAc, 85 : 15). bp 130–132 °C/4 mmHg. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.77 (d, J = 2.2 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.89 (s, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 8.4 Hz, 1H), 7.50 (t, J = 8.1 Hz, 1H), 2.78 (t, J = 7.7 Hz, 2H), 1.75–1.62 (m, 2H), 1.47–1.32 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 152.3, 146.9, 135.5, 134.2, 129.3, 128.6, 128.3, 127.4, 126.6, 33.4, 33.0, 22.4, 14.0. MS: m/z 185 [M]. ^{1}H NMR data are in accordance with literature values.[29]

3-Phenylquinoline

R_f 0.34 (toluene–EtOAc, 85 : 15). bp 169–174 °C/5 mmHg (lit.[30] 205–207 °C/12 mmHg). ^{1}H NMR (300 MHz, CDCl$_3$): δ 9.19 (d, J = 2.3 Hz, 1H), 8.30 (d, J = 2.3 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.88 (dd, J = 1.4, 8.1 Hz, 1H), 7.76–7.69 (m, 3H), 7.61–7.50 (m, 3H), 7.47–7.41 (m, 1H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 150.0, 147.4, 138.0, 133.9, 133.4, 129.5, 129.3, 129.3, 129.3, 128.2, 128.1, 127.5, 127.1. MS: m/z 205 [M]. NMR data are in accordance with literature values.[31]

6-Chloro-3-methylquinoline

R_f 0.50 (toluene–EtOAc, 1 : 1). mp 78–79 °C (EtOH) (lit.[32] 81–82 °C (EtOH)). ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.70 (d, J = 2.1 Hz, 1H), 7.95 (d, J = 9.0 Hz, 1H), 7.73 (s, 1H), 7.63 (s, 1H), 7.52 (dd, J = 2.3, 9.0 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 152.7, 144.9, 133.7, 132.3, 131.6, 130.8, 129.4, 128.7, 125.8, 18.8. MS: m/z 177 [M].

3,6-Dimethylquinoline

R_f 0.47 (toluene–EtOAc, 1 : 1). mp 54–56 °C (lit.[33] 56.5 °C). bp 122–125 °C/8 mmHg. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.67 (d, J = 1.8 Hz, 1H), 7.93 (d, J = 9.1 Hz, 1H), 7.74 (s, 1H), 7.46–7.40 (m, 2H), 2.48 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 151.5, 145.2, 136.3, 134.1, 130.7, 130.4, 128.8, 128.2, 126.0, 21.6, 18.8. MS: m/z 157 [M]. ^{13}C NMR data are in accordance with literature values.[28]

6-Methoxyquinoline

R_f 0.40 (toluene–EtOAc, 1 : 1). bp 129–130 °C/9 mmHg (lit.[34] 153 °C/12 mmHg). ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.76 (dd, J = 1.6, 4.2 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 9.2 Hz, 1H), 7.39–7.32 (m, 2H), 7.07 (d, J = 2.8 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 157.8, 148.1, 144.5, 134.9, 131.0, 129.4, 122.4, 121.5, 105.2, 55.6. MS: m/z 159 [M]. NMR data are in accordance with literature values.[12b]

6-Methoxy-2-methylquinoline

R_f 0.42 (toluene–EtOAc, 1 : 1). bp 130–131 °C/4 mmHg (lit.[35] 145–146 °C/8 mmHg). ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.82 (dd, J = 5.3, 8.7 Hz, 2H), 7.22 (dd, J = 2.8, 9.2 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 6.93 (d, J = 2.8 Hz, 1H), 3.80 (s, 3H), 2.60 (s, 3H).

^{13}C NMR (75 MHz, CDCl$_3$): δ 157.2, 156.4, 144.0, 135.1, 130.1, 127.4, 122.4, 122.0, 105.3, 55.6, 25.2. MS: m/z 173 [M]. NMR data are in accordance with literature values.[36]

6-Methoxy-3-methylquinoline

R_f 0.44 (toluene–EtOAc, 1 : 1). bp 142–143 °C/7 mmHg. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.61 (d, J = 2.0 Hz, 1H), 7.95 (d, J = 9.2 Hz, 1H), 7.80 (s, 1H), 7.29 (dd, J = 2.8, 9.2 Hz, 1H), 6.99 (d, J = 2.7 Hz, 1H), 3.91 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 157.9, 150.0, 142.8, 133.8, 130.9, 130.7, 129.3, 121.3, 104.8, 55.6, 18.9. HRMS: calcd for C$_{11}$H$_{12}$ON: 174.0914 [M+H]$^+$, found: 174.0916.

3-*n*-Butyl-6-methoxyquinoline

R_f 0.61 (toluene–EtOAc, 1 : 1). bp 154–157 °C/6 mmHg. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.61 (d, J = 2.2 Hz, 1H), 7.95 (d, J = 9.2 Hz, 1H), 7.79 (s, 1H), 7.29 (dd, J = 2.8, 9.2 Hz, 1H), 7.01 (d, J = 2.8 Hz, 1H), 3.91 (s, 3H), 2.76 (t, J = 7.7 Hz, 2H), 1.74–1.63 (m, 2H), 1.46–1.33 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 157.9, 149.8, 143.0, 135.8, 133.1, 130.7, 129.3, 121.3, 104.9, 55.6, 33.4, 33.0, 22.4, 14.0. HRMS: calcd for C$_{14}$H$_{18}$ON: 216.1383 [M+H]$^+$, found: 216.1387.

6-Methoxy-3-phenylquinoline

R_f 0.58 (toluene–EtOAc, 1 : 1). mp 119–121 °C (EtOH) (lit.[37] 121–122 °C). ^{1}H NMR (300 MHz, CDCl$_3$): δ 9.03 (d, J = 2.2 Hz, 1H), 8.20 (d, J = 1.8 Hz, 1H), 8.03 (d, J = 9.2 Hz, 1H), 7.73–7.68 (m, 2H), 7.56–7.49 (m, 2H), 7.47–7.35 (m, 2H), 7.13 (d, J = 2.6 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 158.3, 147.5, 143.6, 138.2, 134.3, 132.3, 130.7, 129.3, 129.2, 128.2, 127.6, 122.4, 105.4, 55.7. MS: m/z 235 [M].

3,7-Dimethylquinoline

R_f 0.64 (toluene–EtOAc, 1 : 1). ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.72 (d, J = 2.2 Hz, 1H), 7.87–7.83 (m, 2H), 7.63 (d, J = 8.3 Hz, 1H), 7.34 (dd, J = 1.6, 8.3 Hz, 1H), 2.54 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 152.3, 146.8, 138.6, 134.5, 129.6, 128.9, 128.2, 126.8, 126.2, 21.9, 18.7. MS: m/z 157 [M]. ^{13}C NMR data are in accordance with literature values.[28]

3,5-Dimethylquinoline[38]

R_f 0.60 (toluene–EtOAc, 1 : 1). ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.77 (d, J = 2.1 Hz, 1H), 8.09–8.07 (m, 1H), 7.92 (d, J = 8.6 Hz, 1H), 7.52 (dd, J = 7.0, 8.5 Hz, 1H), 7.39–7.32 (m, 1H), 2.66 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 151.9, 146.9, 133.9, 131.3, 130.1, 129.1, 128.3, 127.5, 127.1, 19.1, 18.7. MS: m/z 157 [M].

3,8-Dimethylquinoline

R_f 0.40 (toluene–EtOAc, 85 : 15). bp 110–120 °C/3 mmHg. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.79 (d, J = 2.3 Hz, 1H), 7.86 (dd, J = 1.0, 2.1 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.48 (d, J = 6.6 Hz, 1H), 7.39 (dd, J = 7.1, 7.9 Hz, 1H), 2.81 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 151.3, 145.7, 136.9, 135.1, 130.2, 128.7, 128.2, 126.4, 125.3, 18.7, 18.2. MS: m/z 157 [M]. ^{13}C NMR data are in accordance with literature values.[28]

8-Chloro-3-methylquinoline

R_f 0.80 (toluene–EtOAc, 1:1). bp 134–137 °C/1.5 mmHg. [1]H
NMR (300 MHz, CDCl$_3$): δ 8.81 (d, J = 2.2 Hz, 1H), 7.85 (dd,
J = 1.0, 2.1 Hz, 1H), 7.69 (dd, J = 1.3, 7.5 Hz, 1H), 7.59 (dd,
J = 1.3, 8.2 Hz, 1H), 7.35 (dd, J = 7.5, 8.1 Hz, 1H), 2.47 (d, J =
0.8 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 152.9, 142.7, 135.1,
133.2, 131.6, 129.5, 128.6, 126.5, 126.4, 18.6. HRMS: calcd for
C$_{10}$H$_9$ClN: 178.0418 [M+H]$^+$, found: 178.0425.

7,8-Benzo-3-methylquinoline

R_f 0.67 (toluene–EtOAc, 85:15). mp 87–88 °C. bp 155–165 °C/4
mmHg. ^{1}H NMR (300 MHz, CDCl$_3$): δ 9.25 (dd, J = 1.4, 8.0 Hz,
1H), 8.85 (d, J = 2.1 Hz, 1H), 7.96 (dd, J = 0.9, 2.0 Hz, 1H), 7.92–
7.88 (m, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.76–7.66 (m, 2H), 7.63 (d,
J = 8.9 Hz, 1H), 2.57 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 150.4,
144.6, 135.3, 133.3, 131.6, 131.4, 127.9, 127.8, 127.8, 127.1, 126.3,
125.2, 124.2, 18.8. HRMS: calcd for C$_{14}$H$_{12}$N: 194.0965 [M+H]$^+$,
found: 194.0958.

5,6-Benzo-3-methylquinoline

R_f 0.56 (toluene–EtOAc, 1:1). mp 81–82 °C (lit.[39] 81.5–82 °C
(heptane)). bp 152–158 °C/5 mmHg. ^{1}H NMR (300 MHz,
CDCl$_3$): δ 8.82 (d, J = 2.1 Hz, 1H), 8.78–8.75 (m, 1H), 8.63 (d, J =
8.0 Hz, 1H), 8.03–7.89 (m, 3H), 7.74–7.60 (m, 2H), 2.63 (s, 3H).
^{13}C NMR (75 MHz, CDCl$_3$): δ 151.3, 146.3, 132.0, 131.0, 130.4,
130.0, 129.6, 128.8, 128.1, 127.3, 127.0, 125.3, 122.7, 19.2. MS:
m/z 193 [M].

4-(Phenylamino)-2-butanone

R_f 0.32 (toluene–EtOAc, 85:15). ^{1}H NMR (300 MHz, CDCl$_3$): δ
7.22–7.14 (m, 2H), 6.71 (dt, J = 1.1, 7.3 Hz, 1H), 6.64–6.58 (m,
2H), 3.42 (t, J = 6.1 Hz, 2H), 2.75 (t, J = 6.1 Hz, 2H), 2.16 (s, 3H).
^{13}C NMR (75 MHz, CDCl$_3$): δ 208.2, 147.8, 129.4, 117.8, 113.2,
42.7, 38.5, 30.5. MS: m/z 163 [M]. NMR data are in accordance
with literature values.[40]

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