# The Rhodium Complex-catalyzed Synthesis of Quinolines from Aminoarenes and Aliphatic Aldehydes

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A variety of aminoarenes react with aliphatic aldehydes in the presence of a catalytic amount of a rhodium complex and an excess amount of the corresponding nitroarenes at 180 °C to give 2-alkyl- and 2,3-dialkyl-substituted quinolines in excellent yields. Among the rhodium complexes examined, $[Rh(norbornadiene)Cl]_2$ exhibits the highest activity as a catalyst. Thus, 2-methyl-, 2-ethyl-3-methyl-, 2-propyl-3-ethyl-, and 2-butyl-3-propylquinoline derivatives are readily obtained from aminoarenes and ethanal, propanal, butanal, and pentanal respectively.

The Skraup and related syntheses are well known as methods for the preparation of quinolines from aminoarenes and carbonyl compounds.[1] These methods, however, have some disadvatages; the uncontrolled violence of the reaction and the use of a large amount of acid. Quinolines can be prepared from aminoarenes and olefins using transition-metal complexes as catalyst precursors.[2,3] Rhodium trichloride catalyzes the reaction between aniline and ethylene to give 2-methylquinoline in poor yields.[2] Octacarbonyldicobalt catalyzes the reaction between *N*-benzylideneaniline and ethyl vinyl ether in tetrahydrofuran under nitrogen to give 2-phenylquinoline in moderate yields.[3] More recently, we found that rhodium complexes such as $\mu,\mu'$-dichlorobis(norbornadiene)dirhodium(I) are active as catalysts for *N*-heterocyclization, the preparation of quinolines from aminoarenes and aliphatic aldehydes in a non-acidic medium.[4] This is a novel method for the preparation of 2-alkyl- and 2,3-dialkyl-substituted quinolines, applicable in a large-scale reaction. Here, a detailed study on the rhodium-catalyzed synthesis of quinolines will be described.

## Results and Discussion

Aniline reacts with aliphatic aldehydes having two α-hydrogens in the presence of a catalytic amount of $\mu,\mu'$-dichlorobis(norbornadiene)dirhodium(I) and an excess amount of nitrobenzene as an oxidizing agent at 180 °C to give alkyl-substituted quinolines in moderate to excellent yields. The results are summarized in Table 1. This provides a convenient method for the synthesis of quinolines.

The combination of aniline with ethanal, propanal, butanal, and pentanal gives 2-methyl-, 2-ethyl-3-methyl-, 2-propyl-3-ethyl-, and 2-butyl-3-propylquinoline, respectively. 2-Methylquinoline was identified by comparing its IR and $^1H$ NMR spectra with those of the authentic sample. None of the $^1H$ NMR spectra (60 MHz in $CDCl_3$, with $Me_4Si$ as the internal standard) of these products exhibited the peak at $\delta$ 8.8 ppm characteristic of the 2-H of the quinoline nucleus.[5] The $^1H$ NMR (60 MHz) spectrum of the product from aniline–propanal showed a typical pattern of the methyl and ethyl groups, while the $^{13}C$ NMR (25.05 MHz) spectrum showed three peaks, at 12.5($CH_3$), 18.7($CH_3$), and 29.1($CH_2$) ppm, in the aliphatic carbon region, assignable to the 2-ethyl(12.5 and 29.1 ppm) and 3-methyl(18.7 ppm) groups. Accordingly, this is concluded to be 2-ethyl-3-methylquinoline.

Alkyl groups of 2,3-disubstituted quinolines produced from butanal and pentanal can be readily identified by means of the $^1H$ NMR (60 and 220 MHz) and $^{13}C$ NMR spectra. The products from aniline–butanal and –pentanal were assigned to 2-propyl(14.4, 22.5, and 37.5 ppm)-3-ethyl(14.4 and 25.0 ppm)quinoline and 2-butyl(14.0, 23.0, 31.7, and 35.4 ppm)-3-propyl-(14.0, 23.5, and 34.3 ppm)quinoline respectively.

The mass spectra of these products exhibited the corresponding molecular ions, and the elemental analysis gave satisfactory results.

The reaction of ethanal gave a considerable amount of a tarry material which appears to reduce the yield of 2-methylquinoline. An attempt of reduce the for-

Table 1. Rhodium-catalyzed synthesis of substituted quinolines from aniline and aldehydes

| Exptl No. | Aldehyde | Product | Yield/%[a] |
|---|---|---|---|
| 1 | Ethanal | 2-Methylquinoline | 51 (30)[b] |
| 2 | Ethanal | 2-Methylquinoline | 14[c] |
| 3 | Ethanal | 2-Methylquinoline | 42[d] |
| 4 | Ethanal | 2-Methylquinoline | 40 |
| 5 | Ethanal | 2-Methylquinoline | 23[e] |
| 6 | Ethanal | 2-Methylquinoline | 17[f] |
| 7 | 2-Butenal | 2-Methylquinoline | Trace |
| 8 | Paraldehyde $(CH_3CHO)_3$ | No reaction | — |
| 9 | Metaldehyde $(CH_3CHO)_4$ | No reaction | — |
| 10 | Propanal | 2-Ethyl-3-methylquinoline | 75 (59) |
| 11 | Butanal | 2-Propyl-3-ethylquinoline | 119 (82) |
| 12 | Pentanal | 2-Butyl-3-propylquinoline | (45) |

Under argon at 180 °C for 4 h. Molar ratio: Aniline (41 mmol)/aldehyde/nitrobenzene = 1.0/2.5/1.5. Rhodium complex: 0.03 mmol$[Rh(NBD)Cl]_2$. Solvent: Ethanol or benzene(20 ml).
a) Determined by GLC. Based on the amount of aniline used. The figures in parentheses show isolated yields. b) Benzene used as solvent. c) At 150 °C. d) Without solvent. e) Acetic acid(4.1 mmol) was added. f) Acetic acid (8.2 mmol) was added.

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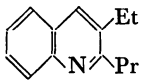
mation of this tarry material was unsuccessful. The reaction at a low temperature (150 °C) or without a solvent gave 2-methylquinoline in poor yields. 2-Butenal gave only a trace of 2-methylquinoline, but a large amount of the tarry material. Paraldehyde [$(CH_3CHO)_3$] and metaldehyde [$(CH_3CHO)_4$] showed no reactivity for this reaction under the conditions used.

On the other hand, propanal, butanal, and pentanal give the corresponding 2,3-disubstituted quinolines in fairly good yields without the formation of any tarry material. The reaction between aniline and butanal was examined in some detail in order to determine the optimum conditions for the preparation of the quinoline; the results are summarized in Table 2. *N*-Butylaniline was formed as a by-product in 5—31% yields. The presence of excess amount of nitrobenzene reduced the formation of *N*-butylaniline. A hydrogen transfer should take place for the formation of the quinoline nucleus.

$$PhNH_2 + 2CH_3CH_2CH_2CHO \xrightarrow[PhNO_2]{[Rh]}$$




$$+ 2H_2O + 2H$$

The nitrobenzene appears to act as an oxidizing agent and to be partially reduced to aniline through the reaction. *N*-Butylaniline appears to be derived *via* *N*-butylideneaniline by hydrogenation. The reaction without nitrobenzene also gave a mixture of *N*-butylaniline and the quinoline, but in poor yields. When the aniline/butanal/nitrobenzene molar ratio is fixed at 1.0/2.2/0.33, the catalytic activity is highest with $\mu,\mu'$-dichlorobis(norbornadiene)dirhodium(I), followed by chlorotris(triphenylphosphine)rhodium(I) and hydridocarbonyltris(triphenylphosphine)rhodium(I).

The catalytic activity also depends on the amounts of the rhodium complex used. With $\mu,\mu'$-dichlorobis(norbornadiene)dirhodium(I), the quinoline yield is highest (119%) when the rhodium catalyst of 0.03 mmol (20 mg) is used. The turn-over of the catalyst is calculated to amount to 1600, based on the yield (119%), and the product selectivity is estimated to be more than 95%, based on the butanal used. Higher (200 °C) or lower (160 °C) temperatures gave poorer yields of the quinoline.

Table 2. The rhodium-catalyzed synthesis of 2-propyl-3-ethylquinoline from aniline and butanal[a]

| | Catalyst[b] | Molar ratio[c] | Product yield[d]/% | |
|---|---|---|---|---|
| | | | 2-Propyl-3-ethyl-quinoline | *N*-Butyl-aniline |
| 1 | A | 1.0/2.2/0.33 | 96 | 31 |
| 2 | A | 1.0/2.2/1.0 | 99 | 20 |
| 3 | A | 1.0/2.5/1.5 | 119 | 5 |
| 4 | B | 1.0/2.2/0.33 | 61 | 10 |
| 5 | C | 1.0/2.2/0.33 | 41 | 7 |
| 6 | A | 1.0/2.5/1.5 | 85[e] | |
| 7 | A | 1.0/2.5/1.5 | 57[f] | |

a) Under argon at 180 °C for 4 h in ethanol(20 ml). b) Rhodium complex, 0.03 mmol. A, $[Rh(NBD)Cl]_2$ (20 mg); B, $RhCl(PPh_3)_3$; C, $RhH(CO)(PPh_3)_3$. c) Molar ratio: Aniline(41 mmol)/butanal/nitrobenzene. d) Determined by GLC. Based on the amount of aniline used. e) $[Rh(NBD)Cl]_2$, 10 mg. f) $[Rh(NBD)Cl]_2$, 5 mg.

Accordingly, the optimum conditions for the preparation of the quinoline are those of Exp. 3 in Table 2. This procedure is applicable for a variety of aniline derivatives combined with ethanal, propanal, and butanal. The reaction between aminoarenes and aldehydes was carried out in the presence of the corresponding nitroarenes as the oxidizing agent. The aminoarene/aldehyde/nitroarene molar ratio was fixed at 1.0/2.5/1.5 in the reaction. The results for *o*- and *p*-substituted anilines including methyl, methoxy, and chloro groups as substituents are summarized in Table 3.

*p*-Methyl-, *p*-methoxy-, and *p*-chloroaniline- reacted smoothly with ethanal, propanal, and butanal to give

Table 3. Synthesis of quinoline derivatives from *o*- and *p*-substituted anilines and aldehydes[a]

| Exptl No. | Aniline | Aldehyde | Product | Yield[b] % |
|---|---|---|---|---|
| 13 | *p*-MeO | Butanal | 2-Propyl-3-ethyl-6-methoxyquinoline | 65 |
| 14 | *p*-MeO | Propanal | 2-Ethyl-3-methyl-6-methoxyquinoline | 70 |
| 15 | *p*-MeO | Ethanal | 6-Methoxy-2-methyl-quinoline | 34 |
| 16 | *p*-Me | Butanal | 2-Propyl-3-ethyl-6-methylquinoline | 60 |
| 17 | *p*-Me | Propanal | 2-Ethyl-3,6-dimethylquinoine | 64 |
| 18 | *p*-Me | Ethanal | 2,6-Dimethylquino-line | 30 |
| 19 | *p*-Cl | Butanal | 2-Propyl-3-ethyl-6-chloroquinoline | 41 |
| 20 | *p*-Cl | Propanal | 2-Ethyl-3-methyl-6-chloroquinoline | 48 |
| 21 | *o*-MeO | Butanal | 2-Propyl-3-ethyl-8-methoxyquinoline | 39 |
| 22 | *o*-MeO | Propanal | 2-Ethyl-3-methyl-8-methoxyquinoline | 25 |
| 23 | *o*-MeO | Ethanal | 8-Methoxy-2-methyl-quinoline | 10 |
| 24 | *o*-Me | Butanal | 2-Propyl-3-ethyl-8-methylquinoline | 59 |
| 25 | *o*-Me | Propanal | 2-Ethyl-3,8-dimethylquinoline | 45 |
| 26 | *o*-Me | Ethanal | 2,8-Dimethyl-quinoline | 24 |
| 27 | *o*-Cl | Butanal | 2-Propyl-3-ethyl-8-chloquinoline | 25 |
| 28 | *o*-Cl | Propanal | 2-Ethyl-3-methyl-8-chloroquinoline | 11 |
| 29 | *o*-Cl | Ethanal | 8-Chloro-2-methyl-quinoline | Trace |

a) Under argon at 180 °C for 4 h. Solvent, ethanol (20 ml). $[Rh(NBD)Cl]_2$; 0.03 mmol(20 mg). Molar ratio: Aminoarene(41 mmol)/aldehyde/nitroarene = 1.0/2.5/1.5. b) Isolated yield based on the amount of aminoarene used.

2,6- or 2,3,6-substituted quinolines in fairly good yields. The reaction of ethanal has an inclination to give poorer yields because of the formation of the tarry material.

*o*-Methyl- and *o*-methoxyaniline also showed a moderate reactivity to give 2,3,8-substituted quinolines in good yields when combined with propanal and butanal. *o*-Chloroaniline, however, gave the product in poor yields, indicating that the chloro group located at the ortho position has an inhibitory effect on the reaction. The combination of *o*-chloroaniline with ethanal failed to give 8-chloro-2-methylquinoline almost entirely.

The results for *m*-methyl-, *m*-methoxy-, and *m*-chloroaniline are summarized in Table 4. These aminoarenes reacted with ethanal, propanal, and butanal to give 2,7-di-, 2,3,5-, and 2,3,7-trisusbtituted quinolines in fairly good yields. From *m*-substituted aminoarenes, two isomeric products are expected to be formed.

The products isolated from *m*-methoxyaniline–ethanal, –propanal, and –butanal were proved by GLC to be pure. Their $^{1}H$ and $^{13}C$ NMR spectra in the aliphatic region exhibited typical patterns of alkyl groups characteristic of 2-methyl, 2-ethyl-3-methyl, and 2-propyl-3-ethyl groups respectively. The $^{1}H$ NMR (220 MHz) spectra of the products from propanal and butanal in the aromatic region showed two singlets and two doublets, assignable to the isomeric 7-substituted quinoline, 2,3,7-substituted ones. The spectrum of the ring hydrogens of the 5-isomers, 2,3,5-substituted ones, should have a different pattern; one singlet, two doublets, and one doublet of doublet. Accordingly, the products from propanal and butanal are identified as 2-ethyl-3-methyl-7-methoxyquinoline and 2-propyl-3-ethyl-7-methoxyquinoline respectively. The $^{1}H$ NMR (220 MHz) spectrum of the product from ethanal exhibited one singlet and four doublets in the aromatic region, asssignable to the 7-isomer.

TABLE 4. SYNTHESIS OF QUINOLINE DERIVATIVES FROM *m*-SUBSTITUTED ANILINES AND ALDEHYDES[a]

| Exptl No. | Aniline | Aldehyde | Yield[b] % | Distribution of products[c] 5-Isomer | 7-Isomer |
|---|---|---|---|---|---|
| 30 | *m*-MeO | Butanal | 44 | 0 | 100 |
| 31 | *m*-MeO | Propanal | 45 | 0 | 100 |
| 32 | *m*-MeO | Ethanal | 26 | 0 | 100 |
| 33 | *m*-Me | Butanal | 68 | 10 | 90 |
| 34 | *m*-Me | Propanal | 62 | 16 | 84 |
| 35 | *m*-Me | Ethanal | 38 | 15 | 85 |
| 36 | *m*-Cl | Butanal | 61 | 18 | 82 |
| 37 | *m*-Cl | Propanal | 55 | 17 | 83 |
| 38 | *m*-Cl | Ethanal | 20 | 18 | 82 |

a) Under argon at 180 °C for 4 h. Solvent, ethanol (20 ml). Rhodium complex; $[Rh(NBD)Cl]_2$, 0.03 mmol(20 mg). Molar ratio; *m*-Aminoarene(41 mmol)/aldehyde/*m*-nitroarene=1.0/2.5/1.5. b) Isolated yield based on the amount of *m*-aminoarene used. c) Determined by GLC. 5-Isomer, 2, 5- or 2, 3, 5-substituted quinolines; 7-isomer, 2, 7- or 2, 3, 7-substituted quinolines.

The 5-isomer from ethanal should have a different pattern; four doublets and one doublet of doublet. Thus, the product from ethanal is identified as 2-methyl-7-methoxyquinoline.

The reaction of *m*-toluidine and *m*-chloroaniline with ethanal, propanal, and butanal appeared to give mixtures of 5- and 7-isomers respectively. The distribution of the two isomers was determined by GLC analysis. The 7-isomers appear to predominate.

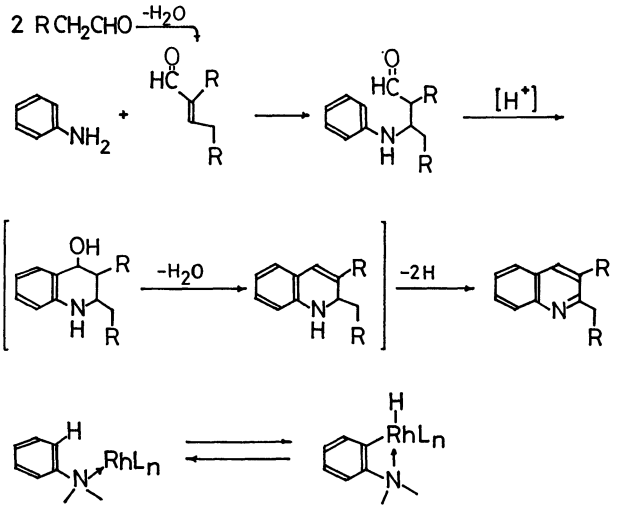
The $^{1}H$ and $^{13}C$ NMR spectra of the products from *m*-toluidine–butanal exhibited the typical pattern of the 7-isomer, assigned to 2-propyl-3-methyl-7-methylquinoline. The $^{13}C$ NMR spectrum clearly showed another pair of peaks with small intensities, assignable to the three alkyl groups (methyl, ethyl, and propyl) in the aliphatic carbon region and the quinoline ring in the aromatic region; nine peaks, five singlets and four doublets by off-resonance decoupling, were observed in the aromatic region. Therefore, the other product is believed to be the 5-isomer, 2-propyl-3-ethyl-5-methylquinoline.

The corresponding 5- and 7-isomers from *m*-toluidine and *m*-chloroaniline, combined with ethanal, propanal or butanal, were similarly analyzed by the spectroscopic method. The fact that the 7-isomers predominate in this procedure is consistent with the finding of the Skraup synthesis, the acid-catalyzed synthesis of quinoline.[6]

The results obtained here clearly demonstrate that the novel *N*-heterocyclization method catalyzed by rhodium complexes in a non-acidic medium is applicable to a veriety of combination of aminoarenes and aldehydes, giving 2-alkyl- and 2,3-dialkyl-substituted quinolines in good to excellent yields.

The Skraup synthesis is generally accepted to follow the following reaction sequence: the self-aldol condensation of aldehyde; the addition of an amine to the condensate, $\alpha,\beta$-unsaturated aldehyde; ring closure by dehydration to form 1,2-dihydroquinoline, and the oxidation of the 1,2-dihydroquinoline. Acids such as concentrated sulfuric acid used as catalysts may participate in the ring-closure process of this sequence.

The mechanism of the rhodium-catalyzed synthesis




Scheme 1.

of quinolines is not yet clear, but the rhodium catalyst also seems to participate in the ring-closure process. Aminoarene reacts with the rhodium catalyst to form an *N*-coordinated complex in which the ortho hydrogen in a phenyl ring of aminoarene can be activated. The *N*-coordinated complex may be transformed into an ortho metallated complex by the intramolecular oxidative addition of the activated C–H bond, for it is the key intermediate for the ring-closure reaction. This consideration may be supported by the fact that triphenylphosphine complexes of iridium[7] and iron[8] give hydridometal complexes, ortho metallated complexes, by intramolecular oxidative addition and the fact that X-ray structures of triphenylphosphine complexes of ruthenium[9] and rhodium[10] reveal a short separation between metal and ortho hydrogen in a phenyl ring of the ligand. Aldehydes with two α-hydrogen atoms have a great tendency to aldol condensation under the conditions used, 180 °C in the presence of a base, suggesting that the formation of α,β-unsaturated aldehydes is also one of the key steps in the reaction. The nitroarenes used may be supposed to act as oxidizing agents in the final step, the oxidation of 1,2-dihydroquinolines.

## Experimental

μ,μ′-Dichlorobis(norbornadiene)dirhodium(I), $[Rh(NBD)Cl]_2$, was prepared according to the method in the literature.[11] The ethanal, propanal, butanal, nitroarenes, aminoarenes, and other compounds employed in this study were all commercial products. The aldehydes, nitroarenes, and aminoarenes were distilled before use. The benzene and ethanol used were dried by the usual methods.

*Analytical Procedure.* The melting points and boiling points are uncorrected. The melting points were taken on a Yanagimoto capillary melting-point apparatus. The infrared spectra were measured on a Hitachi model 215 grating spectrophotometer. The $^1H$ NMR spectra were obtained at 60 MHz with a JEOL LNM-60 NMR or at 220 MHz with a Varian model HR-220 NMR spectrometer. The $^{13}C$ NMR spectra were determined at 25.05 MHz with a JEOL pulsed Fourier Transform spectrometer, model FX-100. Samples were dissolved in $CDCl_3$, and the chemical-shift values were expressed in δ ppm relative to $Me_4Si$ as an internal standard. The mass spectra were recorded on a JMS O1SG mass spectrometer. The elemental analyses were performed at the Microanalytical Center of Kyoto University.

*Reaction Procedure.* A stainless steel autoclave (100 ml) equipped with a magnetic stirrer was used in the reaction. Ethanol (20 ml) and $[Rh(NBD)Cl]_2$ (20 mg, 0.03 mmol) were put into the autoclave. After the air in the autoclave had been replaced with argon, 88—100 mmol of aldehyde, 41 mmol of aminoarene, and 60 mmol of nitroarene were put into it, and then the remainder of the air was replaced with argon. The autoclave was kept at 180 °C by electrical heating for 4 h, and then the heating was turned off. The GLC analysis of the reaction products was made using a column (0.3 cmφ × 3 m) packed with 10% Versamid on Neopak 60—80 mesh. After the solvents had been distilled off, the reaction products were subjected to fractional distillation. 2-Methylquinoline and 2-methyl-6-methoxyquinoline were identified by comparing their IR and $^1H$ NMR spectra with those of authentic samples (Aldrich). The other products were identified by means of the IR, $^1H$ NMR, $^{13}C$ NMR and MS spectra and by elemental analysis. Although the products could not be isolated in an analytically pure form in Exps. 13, 24, 32, 34, and 36, the corresponding quinoline derivatives were identified on the basis of their spectral data.

*2-Ethyl-3-methylquinoline (Exptl 10)*: Yield, 59%; Yellow oil, bp 84—85 °C/0.35 Torr; $^1H$ NMR (60 MHz) ($CDCl_3$): δ (ppm) 1.32 (t, 3H, $CH_3$), 2.25 (s, 3H, $CH_3$), 2.86 (q, 2H, $CH_2$), 7.34—8.09 (m, 5H, Ar). $^{13}C$ NMR (25.05 MHz) ($CDCl_3$): δ (ppm) 12.5 (q, $CH_3$), 18.7 (q, $CH_3$), 29.1 (t, $CH_2$), 125.3 (d), 126.6 (d), 127.1 (s), 128.0 (d), 128.5 (d), 129.0(s), 135.2(d), 146.6(s), 162.5(s), MS (*m/e*): 171 (rel intensity 87, $M^+$), 170(100), 143(43), 115(44). Found: C, 84.28; H, 7.92; N, 8.13%. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18%.

*2-Propyl-3-ethylquinoline (Exptl 11)*: Yield, 82%; Yellow oil, 92 °C/0.3 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): δ (ppm) 1.05 (t, 3H, $CH_3$), 1.25 (t, 3H, $CH_3$), 1.82 (sex, 2H, $CH_2$), 2.73 (q, 2H, $CH_2$), 2.93 (t, 2H, $CH_2$), 7.36 (t, 1H), 7.57 (t, 1H), 7.66 (d, 1H), 7.77 (s, 1H), 8.07 (d, 1H). $^{13}C$ NMR ($CDCl_3$): δ (ppm) 14.2 (q, $CH_3$), 14.4 (q, $CH_3$), 22.5 (t, $CH_2$), 25.0 (t, $CH_2$), 37.5 (t, $CH_2$), 125.3 (d), 126.8 (d), 127.3 (d), 128.1 (s), 128.5 (s), 128.8 (s), 133.1 (s), 135.1 (s). Found: C, 83.78; H, 8.87; N, 6.86%. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03%.

*2-Butyl-3-propylquinoline (Exptl 12)*: Yield, 45%; Yellow oil, 115 °C/0.35 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): δ (ppm) 0.94 (t, 3H, $CH_3$), 0.95 (t, 3H, $CH_3$), 1.46 (sex, 2H, $CH_2$), 1.77 (qt, 2H, $CH_2$), 2.64 (t, 2H, $CH_2$), 2.95 (t, 2H, $CH_2$), 7.68 (s, 1H), 7.59 (d, 1H), 7.34 (t, 1H), 7.52 (t, 1H), 8.05 (d, 1H). $^{13}C$ NMR ($CDCl_3$): δ (ppm) 14.0 (q, $2CH_3$), 23.0 (t, $CH_2$), 23.5 (t, $CH_2$), 31.7 (t, $CH_2$), 34.3 (t, $CH_2$), 35.4 (t, $CH_2$), 125.5(d), 126.8(d), 127.2(s), 128.3(d, d), 133.7(s), 134.8(d), 146.3(s), 161.9(s). MS (*m/e*): 227 (rel intensity 13, $M^+$), 212 (23), 198 (27), 185 (69), 170 (85), 157 (100). Found: C, 84.55; H, 9.58; N, 5.99%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16%.

*2-Propyl-3-ethyl-6-methoxyquinoline (Exptl 13)*: Yield, 65%; Yellow oil, bp 118 °C/0.3 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): δ (ppm) 1.02 (t, 3H, $CH_3$), 1.27 (t, 3H, $CH_3$), 1.77 (sex, 2H, $CH_2$), 2.73 (q, 2H, $CH_2$), 2.91 (t, 2H, $CH_2$), 3.66 (s, 3H, $-OCH_3$), 6.98 (s, 1H), 7.03 (d, 1H), 7.73 (s, 1H), 7.95 (d, 1H). $^{13}C$ NMR ($CDCl_3$): δ (ppm) 14.3 (q, $2CH_3$), 23.0 (t, $CH_2$), 25.0 (t, $CH_2$), 37.2 (t, $CH_2$), 55.4 (q, $-OCH_3$), 104.7(d), 113.9(s), 114.7(d), 121.0(d), 128.2 (s), 129.2(d), 133.3(d), 135.6(s), 157.2(s).

*2-Ethyl-3-methyl-6-methoxyquinoline (Exptl 14)*: Yield, 70%; Yellow oil, bp 98 °C/0.3 Torr; $^1H$ NMR (60 MHz) ($CDCl_3$): δ(ppm) 1.33 (t, 3H, $CH_3$), 2.30 (s, 3H, $CH_3$), 2.87 (q, 2H, $CH_2$), 3.73 (s, 3H, $-OCH_3$), 6.80—8.00 (m, 4H, Ar). Found: C, 77.02; H, 7.88; N, 7.16%. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96%.

*6-Methoxy-2-methylquinoline (Exptl 15)*: Yield, 34%; Yellow oil or yellow crystalline, bp 96 °C/0.4 Torr or mp 63—64 °C; $^1H$ NMR (60 MHz) ($CDCl_3$): δ(ppm) 2.67 (s, 3H, $CH_3$), 3.73 (s, 3H, $-OCH_3$), 6.67—7.93 (m, 5H, Ar). $^{13}C$ NMR ($CDCl_3$): δ(ppm) 24.8 (q, $CH_3$), 55.4 (q, $-OCH_3$), 105.1(d), 121.7(d), 122.0(d), 127.2(s), 129.8(d), 134.8(d), 143.7(s), 155.9(s), 156.9(s). MS (*m/e*): 173 (rel intensity 100, $M^+$), 158 (38), 130 (80), 103 (23), 77 (23). Found: C, 75.37; H, 6.48; N, 5.99%. Calcd for $C_{11}H_{10}NO$: C, 76.28; H, 6.40; N, 6.16%.

*2-Propyl-3-ethyl-6-methylquinoline (Exptl 16)*: Yield, 60%; Yellow oil, bp 96—97 °C/0.2 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): δ(ppm) 1.02 (t, 3H, $CH_3$), 1.14 (t, 3H, $CH_3$), 1.84 (sex, 2H, $CH_2$), 2.30 (s, 3H, $CH_3$), 2.57 (q, 2H, $CH_2$),

2.84 (t, 2H, $CH_2$), 7.50 (s, 1H), 7.23 (s, 1H), 7.25 (s, 1H), 7.93 (d, 1H). $^{13}C$ NMR ($CDCl_3$): $\delta$(ppm) 14.2 (q, $CH_3$), 14.4 (q, $CH_3$), 21.3 (t, $CH_2$), 22.5 (q, $CH_3$), 25.0 (t, $CH_2$), 37.5 (t, $CH_2$), 125.7 (d), 127.3(s), 128.4(s), 130.2(d), 132.7 (d), 134.7(s), 134.9(s), 145.2(s), 160.3(s). MS (*m/e*): 213 (rel int 26, $M^+$), 198 (39), 185 (100), 184 (62). Found: C, 84.44; H, 9.02; N, 6.51%. Calcd for $C_{15}H_{19}N$: C, 84.45; H, 8.98; N, 6.57%.

*2-Ethyl-3-methyl-6-methylquinoline (Exptl 17)*: Yield, 64%; Yellow oil, bp 85—86 °C/0.17 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): $\delta$(ppm) 1.32 (t, 3H, $CH_3$), 2.27 (s, 3H, $CH_3$), 2.30 (s, 3H, $CH_3$), 2.86 (q, 2H, $CH_2$), 7.25 (s, 1H), 7.30 (d, 1H), 7.48 (s, 1H), 7.89 (d, 1H). Found: C, 84.30; H, 8.46; N, 7.24%. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56%.

*2-Propyl-3-ethyl-6-chloroquinoline (Exptl 19)*: Yield, 40%; Yellow oil, bp 101—102 °C/0.2 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): $\delta$(ppm) 1.02 (t, 3H, $CH_3$), 1.25 (t, 3H, $CH_3$), 1.82 (sex, 2H, $CH_2$), 2.73 (q, 2H, $CH_2$), 2.89 (t, 2H, $CH_2$), 7.44 (d, 1H), 7.52 (s, 1H), 7.57 (s, 1H), 7.89 (d, 1H). $^{13}C$ NMR ($CDCl_3$): $\delta$(ppm) 14.1 (q, $CH_3$), 14.3 (q, $CH_3$), 22.5 (t, $CH_2$), 25.0 (t, $CH_2$), 37.4 (t, $CH_2$), 125.5 (d), 127.8(s), 129.0(d), 129.8(d), 131.1(s), 132.8(d), 136.3(s), 144.4(s), 162.1(s). Found: C, 71.74; H, 7.28; N, 5.90; Cl, 15.13%. Calcd for $C_{14}H_{16}NCl$: C, 71.94; H, 6.90; N, 5.99; Cl, 15.17%.

*2-Ethyl-3-methyl-6-chloroquinoline (Exptl 20)*: Yield, 48%; Yellow oil, bp 101—102 °C/0.35 Torr; $^1H$ NMR (60 MHz) ($CDCl_3$): $\delta$(ppm) 1.33(t, 3H, $CH_3$), 2.20(s, 3H, $CH_3$), 2.83 (q, 2H, $CH_2$), 7.20—8.00(m, 4H, Ar). Found: C, 70.04; H, 6.05; N, 6.74; Cl, 17.05%. Calcd for $C_{12}H_{12}NCl$: C, 70.07; H, 5.88; N, 6.81; Cl, 17.24%.

*2-Propyl-3-ethyl-8-methoxyquinoline (Exptl 21)*: Yield, 39%; Yellow oil, bp 116—117 °C/0.2 Torr (mp 63.8—64 °C). $^1H$ NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 1.02(t, 3H, $CH_3$), 1.16 (t, 3H, $CH_3$), 1.84(sex, 2H, $CH_2$), 2.64(q, 2H, $CH_2$), 2.95 (t, 2H, $CH_2$), 3.86(s, 3H, $-OCH_3$), 6.75(d, 1H), 7.16(dt, 2H), 7.61(s, 1H). $^{13}C$ NMR($CDCl_3$): $\delta$(ppm) 14.2(q, $CH_3$), 14.4(q, $CH_3$), 23.0(t, $CH_2$), 25.0(t, $CH_2$), 37.8(t, $CH_2$), 55.8(q, $-OCH_3$), 106.9(d), 118.9(d), 125.5(d), 128.5(s), 133.6(d), 135.6(s), 138.4(s), 155.1(s), 160.5(s). MS(*m/e*): 229(rel int 73, $M^+$), 228(59), 214(36), 201(100), 200(64). Found: C, 77.67; H, 8.31; N, 5.97; O, 7.26%. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11; O, 6.98%.

*2-Ethyl-3-methyl-8-methoxyquinoline (Exptl 22)*: Yield, 25%; Yellow oil, bp 110 °C/0.8 Torr; $^1H$ NMR (60 MHz)($CDCl_3$): $\delta$(ppm) 1.33(t, 3H, $CH_3$), 3.03(q, 2H, $CH_2$), 2.40(s, 3H, $CH_3$), 4.00(s, 3H, $-OCH_3$), 6.67—7.69(m, 4H, Ar). MS (*m/e*): 201(rel int 80, $M^+$), 200(100), 172(47), 171(41). Found: C, 77.51; H, 7.55; N, 7.15; O, 8.25%. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; O, 7.95%.

*8-Methoxy-2-methylquinoline (Exptl 23)*: Yield, 10%; Yellow oil, bp 108 °C/0.8 Torr; $^1H$ NMR (60 MHz)($CDCl_3$): $\delta$(ppm) 2.77(s, 3H, $CH_3$), 4.03(s, 3H, $-OCH_3$), 6.86—8.00(m, 5H, Ar). Found: C, 76.15; H, 6.43; N, 8.19%. Calcd for $C_{11}H_{11}NO$: C, 76.28; H, 6.40; N, 8.09%.

*2-Propyl-3-ethyl-8-methylquinoline (Exptl 24)*: Yield, 59%; Yellow oil, bp 90—92 °C/0.25 Torr; $^1H$ NMR(220 MHz) ($CDCl_3$): $\delta$(ppm) 0.93(t, 3H, $CH_3$), 1.14(t, 3H, $CH_3$), 1.80 (sex, 2H, $CH_2$), 2.61(q, 2H, $CH_2$), 2.66(s, 3H, $CH_3$), 2.82 (t, 2H, $CH_2$), 7.13(t, 1H), 7.32(d, 1H), 7.43(d, 1H), 7.64 (s, 1H). $^{13}C$ NMR($CDCl_3$): $\delta$(ppm) 14.2(q, $2CH_3$), 17.9 (q, $CH_3$), 21.7(t, $CH_2$), 25.0(t, $CH_2$), 37.3(t, $CH_2$), 124.8 (d), 125.1(d), 126.6(s), 127.1(s), 128.2(d), 133.5(d), 134.8 (s), 136.5(s), 159.9(s).

*2-Ethyl-3,8-dimethylquinoline (Exptl 25)*: Yield, 45%; Yellow oil, bp 85 °C/0.25 Torr; $^1H$ NMR(60 MHz)($CDCl_3$): $\delta$(ppm) 1.35(t, 3H, $CH_3$), 2.20(s, 3H, $CH_3$), 2.80(s, 3H, $CH_3$), 2.83(q, 2H, $CH_2$), 7.30—7.50(m, 4H, Ar). $^{13}C$ NMR ($CDCl_3$): $\delta$(ppm) 11.7(q, $CH_3$), 17.8(q, $CH_3$), 18.4(q, $CH_3$), 28.9(t, $CH_2$), 124.6(d), 124.9(d), 126.9(s), 128.0(d), 128.7 (s), 134.9(d), 136.5(s), 145.5(s), 160.6(s). Found: C, 84.05; H, 8.32; N, 7.45%. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56%.

*2-Propyl-3-ethyl-8-chloroquinoline (Exptl 27)*: Yield, 25%; Yellow oil, bp 92 °C/0.35 Torr; $^1H$ NMR(220 MHz)($CDCl_3$): $\delta$(ppm) 1.02(t, 3H, $CH_3$), 1.18(t, 3H, $CH_3$), 1.91(sex, 2H, $CH_2$), 2.61(q, 2H, $CH_2$), 2.86(t, 2H, $CH_2$), 7.16(t, 1H), 7.43(d, 1H), 7.55(d, 1H), 7.60(s, 1H). $^{13}C$ NMR($CDCl_3$): $\delta$(ppm) 19.0(q, $CH_3$), 19.2(q, $CH_3$), 26.9(t, $CH_2$), 29.9 (t, $CH_2$), 42.3(t, $CH_2$), 130.1(d), 130.4(d), 130.9(s), 131.8 (d), 133.1(s), 132.2(d), 138.5(s), 150.5(s), 170.3(s). Found: C, 72.32; H, 7.19; N, 5.94; Cl, 14.19%. Calcd for $C_{14}H_{16}NCl$: C, 71.94; H, 6.89; N, 5.99; Cl, 15.19%. MS (*m/e*): 233(rel int 31, $M^+$), 235(11), 218(48), 205(100), 127(48).

*2-Propyl-3-ethyl-7-methoxyquinoline (Exptl 30)*: Yield, 44%; Yellow oil, bp 122—123 °C/0.38 Torr; $^1H$ NMR (220 MHz) ($CDCl_3$): $\delta$(ppm) 1.02(t, 3H, $CH_3$), 1.16(t, 3H, $CH_3$), 1.82 (sex, 2H, $CH_2$), 2.61(q, 2H, $CH_2$), 2.86(t, 2H, $CH_2$), 7.05 (d, 1H), 7.37(s, 1H), 7.45(d, 1H), 7.57(s, 1H). $^{13}C$ NMR ($CDCl_3$): $\delta$(ppm) 14.2(q, $CH_3$), 14.4(q, $CH_3$), 22.9(t, $CH_2$), 24.9(t, $CH_2$), 37.6(t, $CH_2$), 55.1(q, $-OCH_3$), 106.5(d), 118.5 (d), 122.4(s), 127.8(d), 132.8(s), 133.6(d), 147.8(s), 159.9 (s), 161.7(s). MS(*m/e*): 229 (rel int 52, $M^+$), 214(40), 201 (100), 200(44), 190(62). Found: C, 78.35; H, 8.65; N, 6.22; O, 7.27%. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11; O, 6.98%.

*2-Ethyl-3-methyl-7-methoxyquinoline (Exptl 31)*: Yield, 45%; Yellow oil, bp 99 °C/0.25 Torr; $^1H$ NMR (60 MHz)($CDCl_3$): $\delta$(ppm) 1.27(t, 3H, $CH_3$), 2.23(s, 3H, $CH_3$), 2.87(q, 2H, $CH_2$), 3.73(s, 3H, $-OCH_3$), 6.00—8.00(m, 4H, Ar). Found: C, 77.62; H, 7.23; N, 7.06%. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96%.

*7-Methoxy-2-methylquinoline (Exptl 32)*: Yield, 26%; Yellow oil, bp 90—92 °C/0.7 Torr; $^1H$ NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 2.67(s, 3H, $CH_3$), 3.83(s, 3H, $-OCH_3$), 6.91(d, 1H), 7.02(d, 1H), 7.32(s, 1H), 7.45(d, 1H), 7.73(d, 1H).

*2-Propyl-3-ethyl-7-methylquinoline and 2-propyl-3-ethyl-5-methylquinoline (Exptl 33)*: Yield, 68%; Yellow oil, bp 100—102 °C/0.2 Torr; $^1H$ NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 1.00 (t, 3H, $CH_3$), 1.10(t, 3H, $CH_3$), 1.82(sex, 2H, $CH_2$), 2.30 (s, 3H, $CH_3$), 2.50(q, 2H, $CH_2$), 2.80(t, 2H, $CH_2$), 7.00 (d, 1H), 7.31(d, 1H), 7.43(s, 1H), 7.77(s, 1H). *7-Isomer*: $^{13}C$ NMR ($CDCl_3$): $\delta$(ppm) 14.2(q, $CH_3$), 14.4(q, $CH_3$), 21.6(t, $CH_2$), 22.4(t, $CH_2$), 24.9(t, $CH_2$), 37.4(q, $CH_3$), 125.3(d), 126.5(d), 127.7(d), 133.0(s), 134.1(s), 137.8(s), 146.7(s), 161.1(s). *5-Isomer*; 18.3(q, $CH_3$), 18.7(q, $CH_3$), 21.2(t, $CH_2$), 25.2(t, $CH_2$), 29.2(t, $CH_2$), 36.8(q, $CH_3$), 114.0(d), 116.5(d), 117.2(d), 125.9(d), 127.0(s), 129.3(s), 135.6(s), 143.7(s). Found: C, 84.35; H, 9.02; N, 6.54%. Calcd for $C_{15}H_{19}N$: C, 84.45; H, 8.98; N, 6.56%.

*2-Ethyl-3,7-dimethylquinoline and 2-ethyl-3,5-dimethylquinoline (Exptl 34)*: Yield, 62%; Yellow oil, bp 75 °C/0.35 Torr; $^1H$ NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 1.32(t, 3H, $CH_3$), 2.05(s, 3H, $CH_3$), 2.30(s, 3H, $CH_3$), 2.73 (q, 2H, $CH_2$), 7.00(d, 1H), 7.25(td, 2H), 7.77(s, 1H). $^{13}C$ NMR ($CDCl_3$): $\delta$(ppm) 12.7(q, $CH_3$), 18.8(q, $CH_3$), 21.6(q, $CH_3$), 29.2(t, $CH_2$), 126.2(d), 127.5(d, d), 135.1(d), 128.1(s), 128.8(s), 137.9(s), 146.7(s), 162.6(s). *5-Isomer*; 18.3(q, $CH_3$), 21.1(q, $CH_3$), 26.7(q, $CH_3$), 30.1(t, $CH_2$), 117.4(d), 125.2(d).

*2,7-Dimethylquinoline and 2,5-dimethylquinoline (Exptl 35)*: Yield, 38%; Yellow oil, bp 53—54 °C/0.25 Torr; $^1H$ NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 2.39(s, 3H, $CH_3$), 2.61(s, 3H,

$CH_3$), 7.00(d, 1H), 7.01(d, 1H), 7.45(d, 1H), 7.75(d, 1H), 7.77(s, 1H). *5-Isomer*; 2.45(s, 3H, $CH_3$), 2.62(s, 3H, $CH_3$), 7.00—8.00(m, 5H, Ar). Found: C, 83.80; H, 7.23; N, 8.48%. Calcd for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91%.

*2-Propyl-3-ethyl-7-chloroquinoline (Exptl 36)*: Yield, 61%; Yellow oil, bp 119—120 °C/0.18 Torr; $^1$H NMR (220 MHz) ($CDCl_3$): $\delta$(ppm) 1.00(t, 3H, $CH_3$), 1.18(t, 3H, $CH_3$), 1.77 (sex, 2H, $CH_2$), 2.61(q, 2H, $CH_2$), 2.80(t, 2H, $CH_2$), 7.16 (d, 1H), 7.34(d, 1H), 7.52(s, 1H), 7.91(s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$(ppm) 14.0(q, $CH_3$) 14.3(q, $CH_3$), 22.4(t, $CH_2$), 25.0(t, $CH_2$), 37.5(t, $CH_2$), 125.4(d), 126.3(d), 127.3(d), 127.8(s), 128.0(d), 130.2(s), 133.3(s), 133.8(s), 162.8(s).

*2-Ethyl-3-methyl-7-chloroquinoline (Exptl 37)*: Yield, 55%; Yellow oil or yellow crystalline, bp 95—96 °C/0.25 Torr (mp 54—56 °C). $^1$H NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 1.34(t, 3H, $CH_3$), 2.43(s, 3H, $CH_3$), 3.00(q, 2H, $CH_2$), 7.39(d, 1H), 7.57(d, 1H), 7.80(s, 1H), 8.09(s, 1H). Found: C, 69.88; H, 5.84; N, 6.79; Cl, 17.20%. Calcd for $C_{12}H_{12}NCl$: C, 70.07; H, 5.88; N, 6.81; Cl, 17.24%.

*7-Chloro-2-methylquinoline and 5-Chloro-2-methylquinoline (Exptl 38)*: Yield, 20%; Yellow oil, bp 70—71 °C/0.2 Torr; $^1$H NMR (220 MHz)($CDCl_3$): $\delta$(ppm) 2.63(s, 3H, $CH_3$), 7.09 (d, 1H), 7.25(d, 1H), 7.48(d, 1H), 7.80(d, 1H), 7.93(s, 1H). *5-Isomer*; 2.66(s, 3H, $CH_3$), 7.11(d, 1H), 7.24(d, 1H), 7.45(t, 1H), 7.84(d, 1H), 8.20(d, 1H). Found: C, 67.37; H, 4.57; N, 7.98; Cl, 19.72%. Calcd for $C_{10}H_8NCl$: C, 67.62; H, 4.54; N, 7.89; Cl, 19.95%.

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