Successive substitution of halogen atoms in 4,6-dihaloquinolines in palladium-catalyzed reactions with amines and arylboronic acids

I. P. Beletskaya, A. V. Tsvetkov, P. V. Tsvetkov, G. V. Latyshev, and N. V. Lukashev*

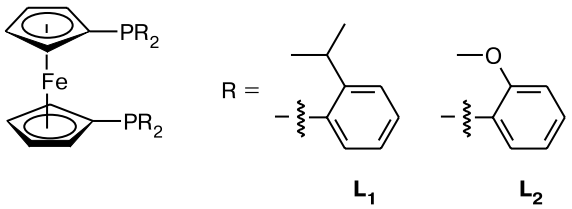
Department of Chemistry, M. V. Lomonosov Moscow State University,
1 Leninskie Gory, 119992 Moscow, Russian Federation.
E-mail: beletska@org.chem.msu.ru

A procedure was developed for the synthesis of 4,6-diamino- and 4,6- or 6,4-arylamino-quinolines by palladium-catalyzed C—N- and/or C—C-cross-coupling of 6-bromo-4-chloroquinoline.

Key words: catalytic amination, 6-bromo-4-chloroquinoline, Suzuki reaction, cross-coupling.

Earlier,[1] we have developed a convenient procedure for the synthesis of 4,6-diarylquinolines, 4,6- and 6,4-arylalkynylquinolines, and 4,6-dialkynylquinolines by the one-pot cross-coupling reaction of 4,6-dihaloquinolines with arylboronic acids and terminal acetylenes. In the present study, this approach was used to prepare 4,6-diaminoquinolines, 6-amino-4-arylquinolines, and 4-amino-6-arylquinolines, which are potentially biologically active compounds (certain aminoquinoline derivatives are known to possess antimalarial[2] and antimicrobial[3] activities and can inhibit kinase[4]). The regioselective introduction of only one group by the cross-coupling reaction can be controlled by the nature of both the halogen atom and the ligand in a palladium complex.

Amination of 6-bromo-4-chloroquinoline (**1**)[5] with a small excess of morpholine was carried out in refluxing dioxane in the presence of sodium *tert*-butoxide and a 2 mol.% palladium catalyst (Scheme 1, Table 1).

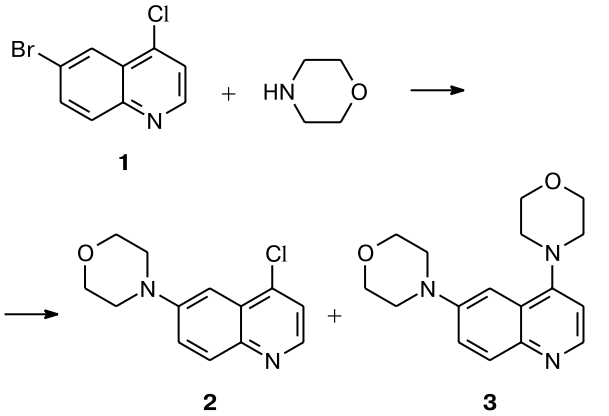


L$_1$ **L**$_2$

We used DPPF and BINAP, which are most commonly used in amination,[6] as the ligands. We also used the ligands **L**$_1$ and **L**$_2$ exhibiting high activity in amination and Suzuki arylation of aryl bromides.*

We found that this substrate is subjected to amination predominantly at the bromine atom. The position of substitution was unambiguously determined from the results of elemental analysis of product **2** and the ^{1}H NMR spectroscopic data. All catalysts provide high selectivity of this process. However, the yield of 6-amino-4-chloroquinoline **2** and the selectivity of the reaction are somewhat higher in the presence of complexes with the ligands **L**$_1$ and **L**$_2$. The use of 4 equiv. of morpholine and an increase in the reaction time to 24 h resulted in the formation of diaminoquinoline **3** as the major product (91% yield).

Scheme 1



Reagents and conditions: 2 mol.% [Pd], Bu^{t}ONa, dioxane, 100 °C, 7 h.

The possibility of amination at the chlorine atom allows for performing the successive one-pot replacement of both halogen atoms in 6-bromo-4-chloroquinoline with different amines (see Scheme 2). The second amine was added to the reaction mixture after completion of the replacement of the bromine atom with the first amine (TLC control). Both reactions afforded diaminoquinolines **4** and **5** in high yields.

* O. V. Gusev, T. A. Peganova, A. M. Kalsin, N. V. Vologdin, P. V. Petrovskii, K. A. Lyssenko, A. V. Tsvetkov, and I. P. Beletskaya, *Organometallics*, 2005, submitted for publication.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 1, pp. 210—214, January, 2005.

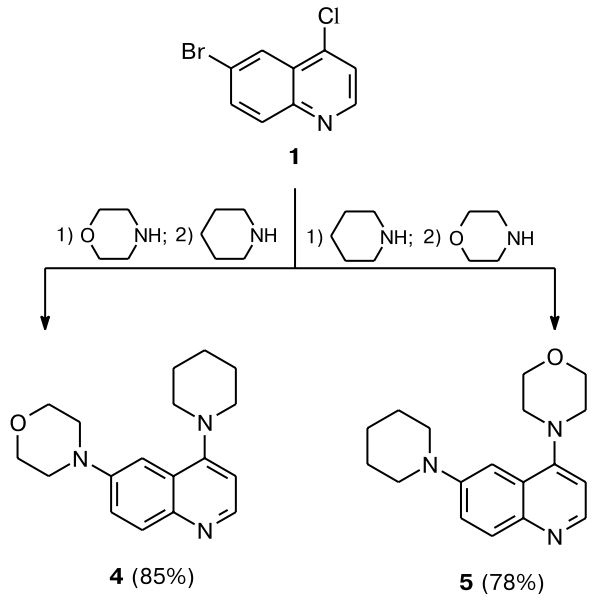
1066-5285/05/5401-0215

Table 1. Ratio between mono- and diamination products prepared by catalytic amination of 6-bromo-4-chloroquinoline with morpholine[a]

Catalyst	Yield[b] (%)	
	2	**3**
$PdCl_2$(dppf)	85	9
$PdCl_2$(**L**$_1$)	93 (92)[c]	5
$PdCl_2$(**L**$_2$)	92	2
$Pd(dba)_2$ + BINAP	84	9

[a] The ratio of 6-bromo-4-chloroquinoline to morpholine is 1 : 1.2.
[b] The ^{1}H NMR spectroscopic data.
[c] Preparative yield.

Scheme 2



Reagents and conditions: 2 mol.%, $PdCl_2$(**L**$_1$), Bu^{t}ONa, dioxane.

A combination of the C—N- and C—C-cross-coupling reactions of dihaloquinoline **1** is another example of the synthetic potential of the methodology under consideration. Its monoamination product **2** was used in the Suzuki reaction with 4-methoxyphenylboronic acid in the presence of palladium complexes (Scheme 3, Table 2).

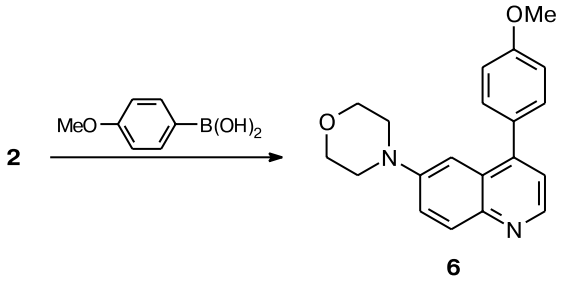
Surprisingly, the $Pd(PPh_3)_4$ complex, which has been earlier demonstrated[1] to be an efficient catalyst for the replacement of the chlorine atom in 6-aryl-4-chloroquinolines by the Suzuki reaction, appeared to be essentially inactive in the case of 4-chloro-6-morpholinoquinoline **2**. A complex with DPPF also proved to be inefficient, and even catalysts with the ligands **L**$_1$ and **L**$_2$ did not give satisfactory results. Apparently, this is associated with the deactivating effect of the amino group as an

Table 2. Catalytic arylation of 4-chloro-6-morpholinoquinoline (**2**) with 4-methoxyphenylboronic acid

Catalyst	Yield[a] of **6** (%)
$Pd(dba)_2$ + BINAP	89 (86)[b]
$PdCl_2$(dppf)	13
$PdCl_2$(**L**$_1$)	54
$PdCl_2$(**L**$_2$)	47
$Pd(PPh_3)_4$	12

[a] The ^{1}H NMR spectroscopic data.
[b] Preparative yield.

Scheme 3



Reagents and conditions: 2 mol.% [Pd], K_2CO_3, dioxane, H_2O, 100 °C, 24 h.

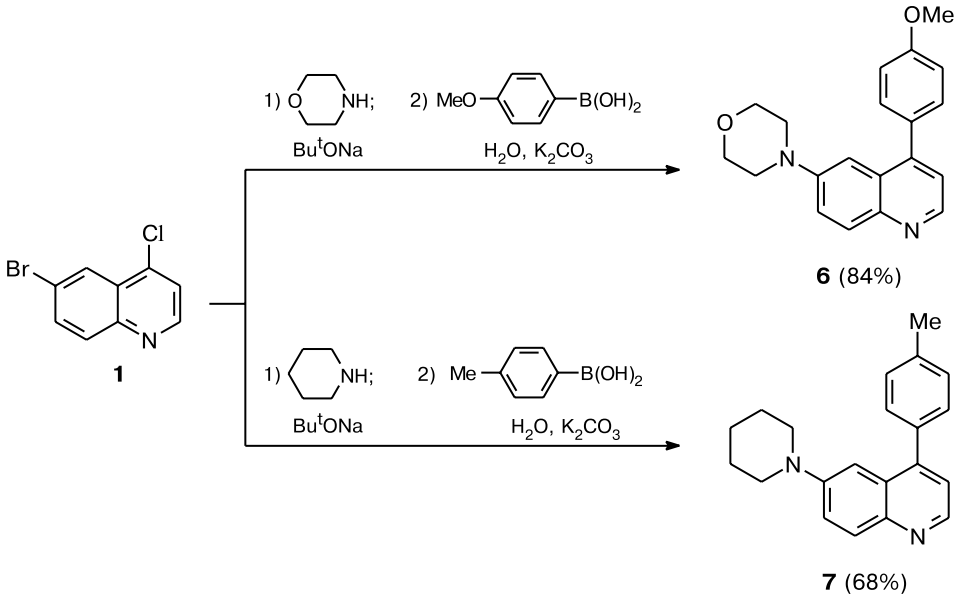
electron-donating substituent. We succeeded in replacing the chlorine atom in high yield only with the use of the $Pd(dba)_2$—BINAP catalytic system. It should be noted that palladium complexes with BINAP are rarely used in the Suzuki reaction.

Successive amination—arylation of 6-bromo-4-chloroquinoline can be carried out in a one-pot fashion without isolation of an intermediate using the $Pd(dba)_2$/BINAP complex as the catalyst for both reactions (Scheme 4). For this purpose, it is necessary to add arylboronic acid, water, and an additional amount of a base to the reaction mixture after completion of the first step (amination at the bromine atom). We used this method for the synthesis of 4-(4-methoxyphenyl)-6-morpholinoquinoline **6** and 6-piperidino-4-(4-tolyl)-quinoline **7** in rather high total yields (84 and 68%, respectively).

It is worthy of note that this approach makes it possible to exclude isolation of an intermediate and decreases the consumption of the catalyst.

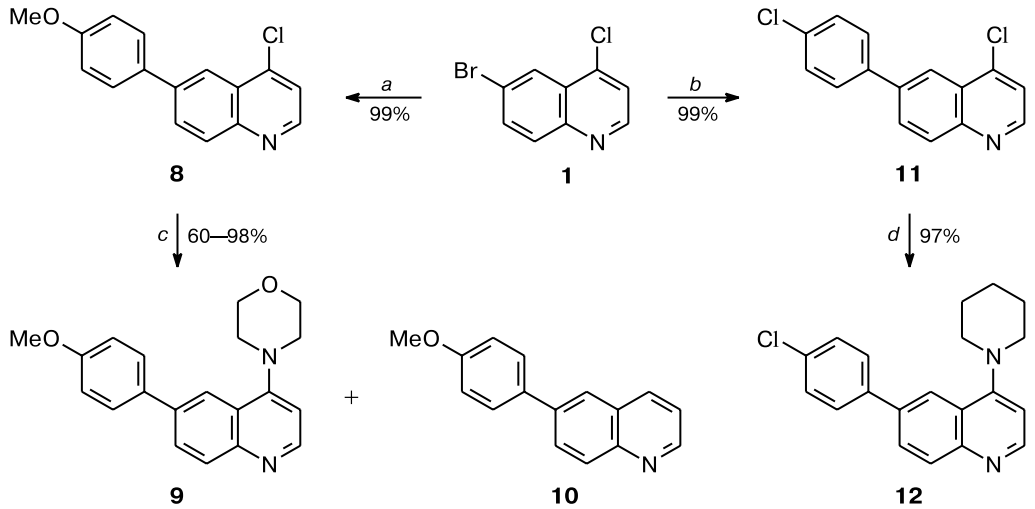
The halogen atoms in 6-bromo-4-chloroquinoline (**1**) can be replaced in another order, *i.e.*, the aryl substituent is initially introduced at position 6 by the Suzuki reaction followed by the introduction of the amino group at position 4 (Scheme 5). The first step of this sequence, *viz.*, Suzuki arylation, was carried out for two substrates, *viz.*,

Scheme 4



Reagents and conditions: 2 mol.%, Pd(dba)$_2$/BINAP, dioxane.

Scheme 5



Reagents and conditions: *a*. 4-MeOC$_6$H$_4$B(OH)$_2$, Pd(PPh$_3$)$_4$, dioxane, H$_2$O, K$_2$CO$_3$, 100 °C, 30 min; *b*. 4-ClC$_6$H$_4$B(OH)$_2$, Pd(PPh$_3$)$_4$, dioxane, H$_2$O, K$_2$CO$_3$, 100 °C, 30 min; *c*. morpholine, [Pd] (see Table 3), Bu^{t}ONa, dioxane, 100 °C, 24 h; *d*. piperidine, PdCl$_2$(**L$_2$**), Bu^{t}ONa, dioxane, 100 °C, 24 h.

4-methoxyphenylboronic acid and 4-chlorophenylboronic acid. The reactions were performed according to our procedure[1] with the use of Pd(PPh$_3$)$_4$ and gave the products in high yields.

Study of the influence of the nature of the catalyst on amination of 4-chloro-6-(4-methoxyphenyl)quinoline **8** with morpholine demonstrated (Table 3) that the reaction involves amination to give product **9** along with reduction of the C—Cl bond to form product **10**. The percentage of the latter increases in the reaction with the use of a DPPF complex. The best results were obtained in the reaction performed in the presence of a complex with the

Table 3. Ratio between amination and reduction products of 4-chloro-6-(4-methoxyphenyl)quinoline **8** prepared by the reaction with morpholine

Catalyst	Conversion (%)	Yield[a] (%)	
		9	**10**
$PdCl_2$dppf	91	60	18
$PdCl_2$(**L₁**)	94	91	3
$PdCl_2$(**L₂**)	100	98 (95)[b]	2
$Pd(dba)_2$ + BINAP	99	95	4

[a] ^{1}H NMR spectroscopic data.
[b] Preparative yield.

ligand **L₂**, which afforded compound **9** in virtually quantitative yield.

Analogously, the reaction in the presence of a catalyst with the ligand **L₂** results in amination of 4-chloroquinoline **11** piperidine to form compound **12** in high yield.

It should be noted that the second chlorine atom in the benzene ring of product **12** is not replaced even with a twofold excess of piperidine.

To summarize, we have demonstrated that various types of compounds can be prepared from 6-bromo-4-chloroquinoline by the one-pot combination of cross-coupling reactions. The results of our study may be of interest for combinatorial chemistry.

Experimental

The reactions were monitored by TLC on Silufol-254 plates and ^{1}H NMR spectroscopy. The yields of amination products of 6-bromo-4-chloroquinoline were determined by ^{1}H NMR spectroscopy (except for experiments, in which the products were isolated preparatively). The ^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian VXR 400 instrument operating at 400 MHz. The chemical shifts are given on the δ scale relative to $(Me_3Si)_2O$. The mass spectra (EI, 70 eV) were measured on a Thermo Finnigan SSQ 7000 mass spectrometer. 6-Bromo-4-chloroquinoline (**1**) was prepared according to a procedure described earlier.[5]

4-Chloro-6-morpholinoquinoline (2). 6-Bromo-4-chloroquinoline (50 mg, 0.206 mmol), morpholine (22 mg, 0.247 mmol, 1.2 equiv.), Bu^{t}ONa (24 mg, 0.247 mmol), a palladium catalyst (0.004 mmol, 2 mol.%) (see Table 1), and dioxane (2.5 mL) were mixed under argon. The reaction mixture was refluxed for 7 h (TLC control), cooled, diluted with CH_2Cl_2, and filtered through a 3-cm silica gel layer. The solution was concentrated under reduced pressure. The product was purified by column chromatography on silica gel (light petroleum—Et_2O, 1 : 1, as the eluent). 4-Chloro-6-morpholinoquinoline **2** was obtained in a yield of 47 mg (92% in the case of the ligand **L₁**), m.p. 98—100 °C. Found (%): C, 62.55; H, 5.45; N, 10.98. $C_{13}H_{13}ClN_2O$. Calculated (%): C, 62.78; H, 5.27; N, 11.26. ^{1}H NMR, δ: 8.55 (d, 1 H, J = 4.69 Hz); 7.98 (d, 1 H, J = 9.38 Hz); 7.49 (dd, 1 H, J = 9.38 Hz, J = 2.64 Hz); 7.34 (d, 1 H, J = 4.69 Hz); 7.34 (d, 1 H, J = 2.64 Hz); 3.91 and 3.33 (both m, 4 H each).

4,6-Bis(morpholino)quinoline (3). 6-Bromo-4-chloroquinoline (50.0 mg, 0.206 mmol), morpholine (72 mg, 0.824 mmol, 4 equiv.), Bu^{t}ONa (60 mg, 0.619 mmol), $PdCl_2$(**L₁**) (3.6 mg, 0.004 mmol), and dioxane (2.5 mL) were mixed under argon in a flask equipped with a reflux condenser. The reaction mixture was refluxed for 24 h (TLC control), cooled, diluted with CH_2Cl_2, and filtered through a 3-cm silica gel layer. The solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel (Et_3N—CH_2Cl_2, 1 : 50, as the eluent). 4,6-Bis(morpholino)quinoline (**3**) was obtained in a yield of 56 mg (91%), m.p. 140—141 °C. Found (%): C, 68.04; H, 7.20; N, 14.09. $C_{17}H_{21}N_3O_2$. Calculated (%): C, 68.20; H, 7.07; N, 14.04. ^{1}H NMR, δ: 8.59 (d, 1 H, J = 4.98 Hz); 7.96 (d, 1 H, J = 9.38 Hz); 7.42 (dd, 1 H, J = 9.38 Hz, J = 2.83 Hz); 7.23 (d, 1 H, J = 2.83 Hz); 6.82 (d, 1 H, J = 4.99 Hz); 3.97, 3.92, 3.26, and 3.19 (all m, 4 H each).

6-Morpholino-4-piperidinoquinoline (4). 6-Bromo-4-chloroquinoline (50 mg, 0.206 mmol), morpholine (19 mg, 0.216 mmol), Bu^{t}ONa (59 mg, 0.618 mmol), $PdCl_2$(**L₁**) (3.6 mg, 0.004 mmol) and dioxane (2.5 mL) were mixed under argon in a flask equipped with a reflux condenser. The reaction mixture was refluxed for 7 h (TLC control). Then piperidine (53 mg, 0.624 mmol) was added, after which the reaction mixture was refluxed for 24 h (TLC control), cooled, diluted with CH_2Cl_2, and filtered through a 3-cm silica gel layer. The solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel (Et_3N—CH_2Cl_2, 1 : 50, as the eluent). 6-Morpholino-4-piperidinoquinoline (**4**) was obtained in a yield of 52 mg (85%), m.p. 120—121 °C. Found (%): C, 72.68; H, 7.79; N, 14.34. $C_{18}H_{23}N_3O$. Calculated (%): C, 72.70; H, 7.80; N, 14.13. ^{1}H NMR, δ: 8.54 (d, 1 H, J = 4.98 Hz); 7.93 (d, 1 H, J = 9.09 Hz); 7.39 (dd, 1 H, J = 9.09 Hz, J = 2.64 Hz); 7.23 (d, 1 H, J = 2.64 Hz); 6.78 (d, 1 H, J = 4.98 Hz); 3.91, 3.26, 3.14, and 1.83 (all m, 4 H each); 1.70 (m, 2 H).

4-Morpholino-6-piperidinoquinoline (5) was prepared analogously from 6-bromo-4-chloroquinoline (50 mg) in a yield of 48 mg (78%), oil. ^{1}H NMR, δ: 8.55 (d, 1 H, J = 4.86 Hz); 7.91 (d, 1 H, J = 9.37 Hz); 7.44 (dd, 1 H, J = 9.37 Hz, J = 2.71 Hz); 7.21 (d, 1 H, J = 2.71 Hz); 6.79 (d, 1 H, J = 4.86 Hz); 3.97, 3.25, 3.17, and 1.76 (all m, 4 H each); 1.63 (m, 2 H). MS (70 eV, m/z): 297 $[M]^+$ (100); 181 (17); 238 (18); 207 (33); 183 (21); 155 (15); 91 (9); 49 (10).

4-(4-Methoxyphenyl)-6-morpholinoquinoline (6). ***A.*** 4-Chloro-6-morpholinoquinoline (**2**) (15 mg, 0.06 mmol), 4-methoxyphenylboronic acid (14 mg, 0.09 mmol, 1.5 equiv.), K_2CO_3 (25 mg, 0.18 mmol), a palladium catalyst (0.001 mmol, 2 mol.%) (see Table 2), and dioxane (2.5 mL, 0.5 mL) were mixed under argon. The reaction mixture was refluxed for 24 h (TLC control), cooled, diluted with CH_2Cl_2, and filtered through a 3-cm silica gel layer. The solution was concentrated under reduced pressure. Column chromatography on silica gel (light petroleum—Et_2O, 1 : 1, as the eluent) afforded 4-(4-methoxyphenyl)-6-morpholinoquinoline (**6**) in a yield of 17 mg (86% for the BINAP catalyst), oil. ^{1}H NMR, δ: 8.71 (d, 1 H, J = 4.40 Hz); 8.04 (d, 1 H, J = 9.38 Hz); 7.45 (dd, 1 H, J = 9.38 Hz, J = 2.64 Hz); 7.21 (d, 1 H, J = 4.40 Hz); 7.17 (d, 1 H, J = 2.64 Hz); 7.44 and 7.04 (both m, 2H each); 3.89 (s, 3 H); 3.84 and 3.16 (both m, 4 H each). MS (70 eV, m/z): 320 $[M]^+$ (100);

289 (6); 281 (6); 262 (78); 234 (5); 218 (7); 207 (13); 191 (25); 109 (7); 96 (9).

B. 6-Bromo-4-chloroquinoline (50 mg, 0.206 mmol), morpholine (21 mg, 0.237 mmol), Bu^tONa (23 mg, 0.237 mmol), $Pd(dba)_2$ (2.3 mg, 0.004 mmol), BINAP (2.5 mg, 0.004 mmol), and dioxane (2.5 mL) were mixed under argon. The reaction mixture was refluxed for 7 h until 6-bromo-4-chloroquinoline disappeared (TLC control). Then 4-methoxyphenylboronic acid (63 mg, 0.412 mmol), K_2CO_3 (115 mg, 0.824 mmol), and water (0.5 mL) were added, and the mixture was refluxed until the reaction was completed (24 h, TLC control). Product **6** was isolated as described in the method ***A***. The yield was 55 mg (84%).

4-(4-Methylphenyl)-6-piperidinoquinoline (7) was prepared analogously to compound **6** (method ***B***) from 6-bromo-4-chloroquinoline (50 mg, 0.206 mmol), piperidine (20 mg, 0.237 mmol), and 4-methylphenylboronic acid (56 mg, 0.412 mmol). The yield was 42 mg (68%), oil. ^{1}H NMR, δ: 8.68 (d, 1 H, J = 4.39 Hz); 7.98 (d, 1 H, J = 9.08 Hz); 7.49 (dd, 1 H, J = 9.08 Hz, J = 2.63 Hz); 7.18 (d, 1 H, J = 4.39 Hz); 7.16 (d, 1 H, J = 2.63 Hz); 7.40 and 7.31 (both m, 2 H each); 3.15 (m, 4 H); 2.45 (s, 3 H); 1.68 (m, 4 H); 1.57 (m, 2 H). MS (70 eV, m/z): 302 $[M]^+$ (100); 287 (4); 246 (7); 217 (12); 189 (4); 123 (7); 109 (8); 32 (3).

4-Chloro-6-(4-methoxyphenyl)quinoline (8). 6-Bromo-4-chloroquinoline (50 mg, 0.206 mmol), 4-methoxyphenylboronic acid (31 mg, 0.206 mmol), K_2CO_3 (85 mg, 0.618 mmol), $Pd(PPh_3)_4$ (4.7 mg, 0.004 mmol), dioxane (2.5 mL), and water (0.5 mL) were mixed under argon in a flask equipped with a reflux condenser. The reaction mixture was refluxed for 30 min (TLC control), cooled, diluted with CH_2Cl_2, and filtered through a 3-cm silica gel layer. The solution was concentrated under reduced pressure. Column chromatography (light petroleum—Et_2O, 1 : 1, as the eluent) afforded 4-chloro-6-(4-methoxyphenyl)quinoline (**8**) in a yield of 55 mg (99%), m.p. 112—113 °C. Found (%): C, 71.44; H, 4.39; N, 4.98. $C_{16}H_{12}ClNO$. Calculated (%): C, 71.25; H, 4.48; N, 5.19. ^{1}H NMR, δ: 8.73 (d, 1 H, J = 4.7 Hz); 8.33 (d, 1 H, J = 2.1 Hz); 8.15 (d, 1 H, J = 8.8 Hz); 7.98 (dd, 1 H, J = 8.8 Hz, J = 2.1 Hz); 7.66 (m, 2 H); 7.47 (d, 1 H, J = 4.7 Hz); 7.02 (m, 2 H); 3.86 (s, 3 H).

4-Chloro-6-(4-chlorophenyl)quinoline (11) was prepared analogously to compound **8** from 6-bromo-4-chloroquinoline (50 mg, 0.206 mmol) and 4-chlorophenylboronic acid (32 mg, 0.206 mmol) in a yield of 56 mg (99%), m.p. 115—116 °C. Found (%): C, 66.12; H, 3.57; N, 5.00. $C_{15}H_{29}Cl_2N$. Calculated (%): C, 65.72; H, 3.31; N, 5.11. ^{1}H NMR, δ: 8.89 (d, 1 H, J = 4.4 Hz); 8.41 (d, 1 H, J = 2.4 Hz); 8.20 (d, 1 H, J = 9.1 Hz); 7.95 (dd, 1 H, J = 9.1 Hz, J = 2.4 Hz); 7.47 (m, 2 H); 7.40 (d, 1 H, J = 4.4 Hz); 7.36 (m, 2 H).

6-(4-Methoxyphenyl)-4-morpholinoquinoline (9). 4-Chloro-6-(4-methoxyphenyl)quinoline (**8**) (50 mg, 0.186 mmol), morpholine (20 mg, 0.233 mmol, 1.25 equiv.), Bu^tONa (22 mg, 0.233 mmol), a 2 mol.% palladium catalyst (see Table 3), and dioxane (2.5 mL) were mixed under argon in a flask equipped with a reflux condenser. The reaction mixture was refluxed for 24 h (TLC control), cooled, diluted with CH_2Cl_2, and filtered through a 3-cm silica gel layer. The solution was concentrated under reduced pressure. Column chromatography (light petroleum—Et_2O, 1 : 1, as the eluent) afforded 6-(4-methoxyphenyl)-4-morpholinoquinoline **9** in a yield of 56 mg (95% in the case of the ligand $\mathbf{L_2}$), m.p. 155—156 °C. Found (%): C, 74.68; H, 6.32; N, 8.52. $C_{20}H_{20}N_2O_2$. Calculated (%): C, 74.98; H, 6.29; N, 8.74. ^{1}H NMR, δ: 8.70 (d, 1 H, J = 4.98 Hz); 8.12 (d, 1 H, J = 2.05 Hz); 8.09 (d, 1 H, J = 8.79 Hz); 7.87 (dd, 1 H, J = 8.79 Hz, J = 2.05 Hz); 7.61 and 7.02 (both m, 2 H each); 6.84 (d, 1 H, J = 4.98 Hz); 8.97 (m, 4 H); 3.85 (s, 3 H); 3.22 (m, 4 H).

6-(4-Chlorophenyl)-4-piperidinoquinoline (12) was prepared analogously to compound **9** (catalyst with the ligand $\mathbf{L_2}$) starting from 4-chloro-6-(4-chlorophenyl)quinoline **11** (50 mg) and piperidine in a yield of 57 mg (97%), oil. ^{1}H NMR, δ: 8.68 (d, 1 H, J = 4.98 Hz); 8.13 (d, 1 H, J = 2.05 Hz); 8.10 (d, 1 H, J = 8.79 Hz); 7.83 (dd, 1 H, J = 8.79 Hz, J = 2.05 Hz); 7.60, 7.40 (both m, 2 H each); 6.82 (d, 1 H, J = 4.98 Hz); 3.23, 1.85 (both m, 4 H each); 1.71 (m, 2 H). MS (70 eV, m/z): 322 $[M]^+$ (100); 265 (12); 239 (5); 204 (7); 176 (24); 119 (8); 102 (9); 88 (13).

This study was financially supported by the Russian Foundation for Basic Research (Project Nos 01-03-33144 and 04-03-32995).

References

1. (a) I. P. Beletskaya, A. V. Tsvetkov, G. V. Latyshev, and N. V. Lukashev, *Zh. Org. Khim.*, 2003, **39**, 1660 [*Russ. J. Org. Chem.*, 2003, **39** (Engl. Transl.)]; (b) A. V. Tsvetkov, G. V. Latyshev, N. V. Lukashev, and I. P. Beletskaya, *Tetrahedron Lett.*, 2002, **43**, 7267; (c) I. P. Beletskaya, G. V. Latyshev, A. V. Tsvetkov, and N. V. Lukashev, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 181 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 189].
2. (a) C. C. Price and R. M. Roberts, *J. Am. Chem. Soc.*, 1946, **68**, 1204; (b) D. E. Pearson, W. H. Jones, and A. C. Cope, *J. Am. Chem. Soc.*, 1946, **68**, 1225.
3. (a) M. Ya. Uritskaya, O. S. Anisimova, I. S. Tubina, T. Yu. Vinokurova, G. N. Permin, N. Yu. Moskolenko, T. L. Gus´kova, S. N. Kutchak, L. F. Setevaev, N. D. Sokolova, S. A. Shareva, L. A. Checherina, and L. N. Yakhontov, *Khim.-farm. Zh.*, 1983, **17**, 1334 [*Pharm. Chem. J.*, 1983, **17** (Engl. Transl.)]; (b) M. V. Rubtsov, C. N. Pershin, N. A. Yanbukin, L. A. Pelenitsina, T. J. Gurevich, N. A. Novitskaya, S. N. Milovanova, and S. A. Vichkanova, *J. Med. Pharm. Chem.*, 1960, **2**, 113.
4. D. H. Boshelli, Ye Fei, Y. D. Wang, M. Dutia, S. L. Johnson, Wu Bigi, K. Muller, D. W. Powell, D. Yaczko, M. Young, M. Tischer, K. Arndt, C. Diseafani, C. Etienne, J. Cibbons, J. Crod, J. Lucas, J. M. Weber, and F. Boschelli, *J. Med. Chem.*, 2001, **44**, 3965.
5. N. J. Leonard and S. N. Boyd, Jr., *J. Org. Chem.*, 1946, **11**, 419.
6. (a) B. H. Yang and S. L. Buchwald, *J. Organomet. Chem.*, 1999, **576**, 125; (b) J. F. Hartwig, *Angew. Chem., Int. Ed.*, 1998, **37**, 2046.

Received November 19, 2004