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Synthesis of 6-methoxy-N^2,N^2,N^4,N^4,N^5,N^5-hexamethylquinoline-2,4,5-triamine – a new representative of quinoline proton sponges

Olga V. Dyablo[1]*, Alexander F. Pozharskii[1], Elena A. Shmoilova[1], Aleksey O. Savchenko[1]

[1] *Southern Federal University, 7 Zorge St., Rostov-on-Don 344090, Russia; e-mail: dyablo@sfedu.ru; apozharskii@sfedu.ru*

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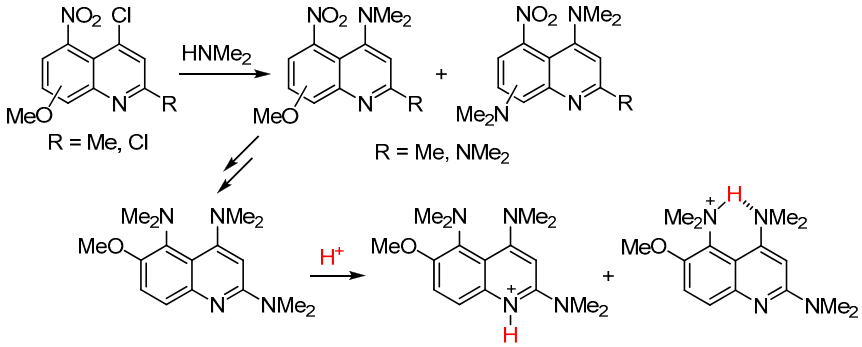


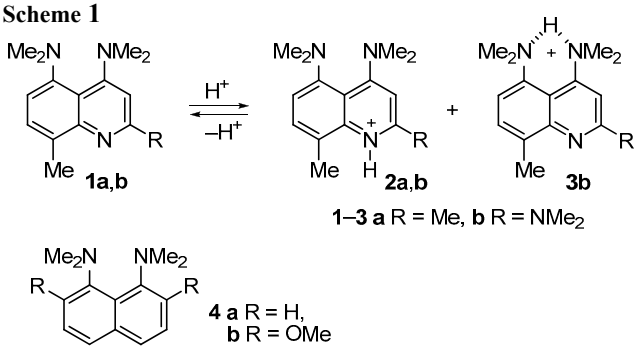
We report the synthesis of 4-chloro-2-methyl-5-nitro- and 2,4-dichloro-5-nitroquinolines, containing methoxy groups at positions 6 and 8. The reaction of these compounds with dimethylamine solution in alcohol was shown to produce not only aminodehalogenation products, but also resulted in nucleophilic substitution of the methoxy groups. The reduction of 6-methoxy-N^2,N^2,N^4,N^4-tetramethyl-5-nitroquinoline-2,4-diamine with subsequent methylation gave 6-methoxy-N^2,N^2,N^4,N^4,N^5,N^5-hexamethylquinoline-2,4,5-triamine, a new representative of quinoline proton sponges.

Keywords: 1,8-bis(dimethylamino)naphthaline, 6-methoxy-N^2,N^2,N^4,N^4,N^5,N^5-hexamethylquinoline-2,4,5-triamine, 4-chloro-5-nitroquinoline, aminodehalogenation, nitration, proton sponge.

Recently we reported a synthesis of the first two 4,5-bis(dimethylamino)quinolines **1a**,**b**,[1,2] which can be considered as quinoline analogs of 1,8-bis(dimethylamino)-naphthaline (**4a**) (proton sponge[3]). Both compounds **1a**,**b** showed a lower basicity (by 0.3–1.2 pK_a units) than diamine **4a**, as expected due to the electron-withdrawing nature of the aza substituent. Most remarkably, these compounds underwent two types of protonation. While compound **1a** in solution or solid state was always protonated as azine, forming the cation **2a** (Scheme 1), the derivative **1b** having a 2-NMe_2 group was protonated simultaneously both as azine and a proton sponge. Thus, its salts existed in solid state as the chelated cation **3b**, while both forms **2b** and **3b** were formed in solution, at a ratio depending on the polarity of solvent.[1]

The nearly half a century study of proton sponges has been focused on searching of stronger bases and achieving a better understanding of the relationship between their structure and basicity.[3,4] One of the first ideas in this direction was to take advantage of the so-called buttressing

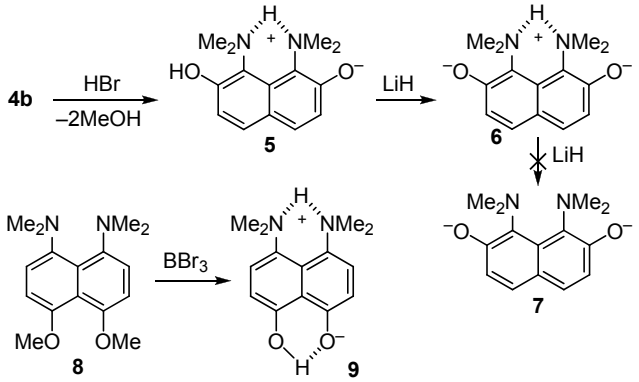
Scheme 1



effect.[5–7] Since the unusually strong basicity of proton sponge (pK_a 12.10, H_2O;[8] pK_a 18.62, MeCN[9]) is explained by the destabilization of free base by the considerable electrostatic repulsion between the lone electron pairs of *peri*-dimethylamino groups, additional destabilization of the base was proposed through introducing bulky substituents, especially with lone electron pairs, at the *ortho* positions relative to the dimethylamino groups.

These expectations were quite justified (some exceptions have been described[7]) in the case of 1,8-bis-(dimethylamino)-2,7-dimethoxynaphthaline (**4b**), the pK_a value of which is 16.3 (in H_2O). For a long time this was the strongest known base among neutral organic molecules.[5,6] We should note that demethylation of compound **4b** with HBr gives 2,7-binaphthol, which exists as betaine **5** (Scheme 2). Treatment with lithium hydride in DMSO leads only to deprotonation of a second OH group and the formation of dinaphtholate **6**, holding a strongly chelated proton that could not be removed even after prolonged heating with lithium hydride.

Scheme 2

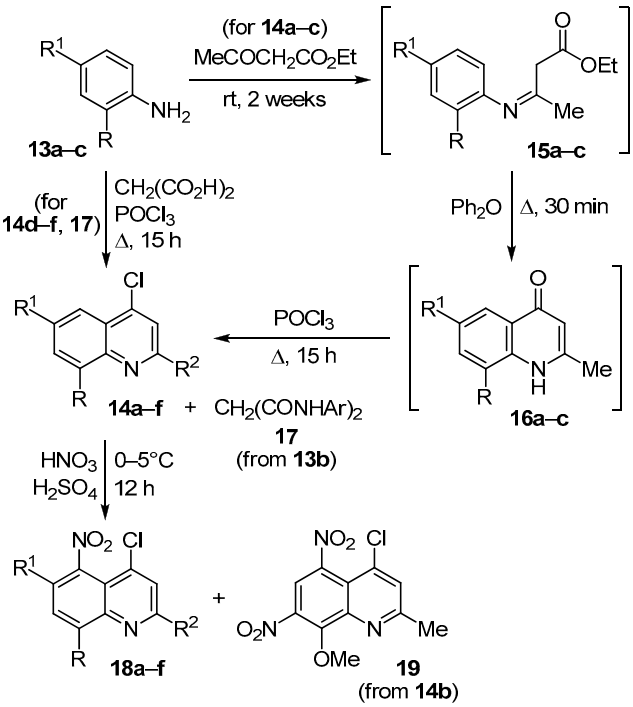


The pK_a value of dianion **7** was estimated to be significantly above 25, making it the strongest currently known arylamine base.[10] The demethylation of 4,5-dimethoxy derivative of proton sponge **8** similarly produced the betaine **9** (Scheme 2), featuring a symmetrical hydrogen N–H···N bond and an asymmetric O–H···O bond.[11]

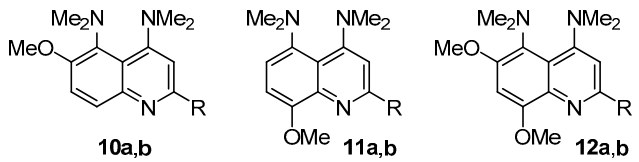
When taking into account all these facts, we decided to prepare methoxy derivatives of quinoline proton sponge in order to obtain increased basicity and to shift the protonation towards dimethylamino groups. We should note that the introduction of two dimethylamino groups at the *peri* positions is quite difficult due to electronic asymmetry of the quinoline system,[2] therefore such syntheses require many stages and seldom are selective. In the current work, we aimed to find methods for the synthesis of methoxy derivatives **10**–**12** from *ortho*-anisidine (**13b**), *para*-anisidine (**13a**), or 2,4-dimethoxyaniline (**13c**), respectively.

We assumed that cyclization of methoxyanilines **13a**–**c** according to the Conrad–Limpach method[12,13] would allow to obtain 4-chloro-2-methylquinolines **14a**–**c**. Indeed, the condensation of methoxyanilines **13a**–**c** with acetoacetic ester, followed by heating of the azomethine intermediates **15a**–**c** in diphenyl ether resulted in the formation of quinolones **16a**–**c** (Scheme 3). The latter were further treated without purification by heating with $POCl_3$, resulting in the preparation of compounds **14a**–**c**, albeit in yields not exceeding 31%, as calculated from the starting methoxyanilines **13**.

Scheme 3



13, **15**, **16** **a** R = H, R^1 = OMe, **b** R = OMe, R^1 = H, **c** R = R^1 = OMe;
14, **18** **a** R = H, R^1 = OMe, R^2 = Me, **b** R = OMe, R^1 = H, R^2 = Me,
c R = R^1 = OMe, R^2 = Me, **d** R = H, R^1 = OMe, R^2 = Cl,
e R = OMe, R^1 = H, R^2 = Cl, **f** R = R^1 = OMe, R^2 = Cl



10–**12** **a** R = Me, **b** R = NMe_2

The 2,4-dichloroquinolines **14d**–**f** were obtained according to method proposed by Ziegler and Gelfert.[14] The reaction of anilines **13a**–**c** with malonic acid in $POCl_3$ medium gave 2,4-dichloroquinolines **14d**–**f** in 12–50% yields (Scheme 3). In the case of *ortho*-anisidine (**13b**) reaction with malonic acid, the malonic diamide **17** was isolated from reaction mixture as by-product.

It is known that mononitration of quinolines with electron-donating substituents at positions 6 or 8 occurs exclusively at position 5. Such examples reported in the literature include 6-alkyl-,[15] 2,6-dimethyl-,[16] 4-chloro-6-methyl-,[17] 4-chloro-6-methoxy-,[17] 4-chloro-6,8-dimethoxy-,[17] 2-iodo-6-methoxy-,[18] 4-chloro-8-methoxy-,[17] and 2-cyano-8-hydroxyquinolines.[19] We performed nitration of 4-chloroquinoline methoxy derivatives **14a**–**f** with 10% excess of nitrating mixture at 0–5°C and observed similar results, obtaining the respective mononitro derivatives **18a**–**f** in moderate to good yields (37–87%) (Scheme 3). Only when nitrating the quinoline **14b**, 5,7-dinitro derivative **19** was isolated as minor product in approximately 5% yield. The moderate yields in some experiments correlated with the significant resinification formation of the reaction mixture.

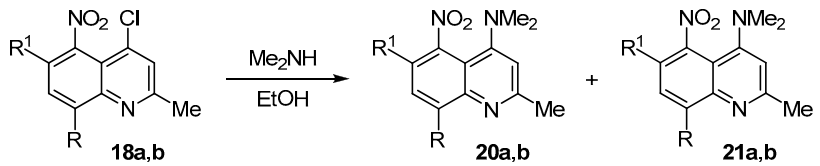
The structures of all nitro derivatives **18** were confirmed by spectral methods. In the case of 6-methoxy derivatives **18a**,**d**, the appearance of aromatic ^{1}H NMR signals (two doublets with coupling constant ^3J = 9.4 Hz) clearly indicated the presence of nitro group at position 5. On the other hand, the nitration products obtained from quinolines **14b**,**e** could be either 4-chloro-5-nitroquinolines **18b**,**e** or the isomeric 7-nitro derivatives, according to ^{1}H NMR spectra. The formation of products due to substitution at position 5 was indirectly evidenced by the significant decrease of ^{1}H NMR coupling constants of aromatic protons (8.5–8.6 Hz) compared to the analogous coupling constants in 6-methoxy derivatives **18a**,**d** (9.4 Hz). A clear indication of 5-nitro isomer was obtained from NOESY spectrum of compound **18b**, which contained a cross peak between the protons of 8-OCH_3 group and the aromatic H-7 proton. Since the substitution in monomethoxy derivatives occurred exclusively at position 5, the substitution in 6,8-dimethoxyquinolines **14c**,**f** apparently should also lead to 5-nitro derivatives, especially since position 5 in these compounds is sterically less crowded.

We further found that the treatment of compounds **18a**–**f** with dimethylamine solution in alcohol led to nucleophilic substitution of not only chlorine atom, but also the methoxy group, activated by nitro group and the ring nitrogen atom. The direction of substitution here was substantially affected by the substrate structure and the reaction temperature. This observation was in line with a previous report,[17] where greater lability of methoxy group compared to chlorine atom was described in the case of 4-chloro-8-methoxy-5-nitroquinoline amination with *N*,*N*-dimethylpropane-1,3-diamine.

For example, both the chlorine atom and methoxy group in 4-chloro-2-methyl-5-nitroquinolines **18a**,**b** were easily substituted with dimethylamino group (Scheme 4, Table 1). However, while the monoamination product **20b** could be isolated from the reaction of 8-methoxy derivative **18b** at room temperature (Table 1, experiment 5), the only product from the reaction of 6-methoxy isomer **18a** with dimethylamine under analogous conditions was 4,6-bis(dimethylamino)quinoline **21a** (Table 1, experiment 3). Only after maintaining the reaction mixture at 5°C (Table 1, experiment 2), trace amounts of the amine **20a** were observed by ^{1}H NMR spectroscopy along with unreacted starting material. It should be noted that the reactions with dimethylamine were accompanied by significant formation of intractable products, probably due to the increased contribution of quinoid structures, caused by conjugation of methoxy and nitro groups. This, in turn, may facilitate the addition of dimethylamine at C(7)–C(8) or C(6)–C(7) bonds of compounds **18a** and **18b**, respectively, giving unstable adducts.

Depending on the reaction conditions, 2,4-dichloro-6(8)-methoxy-5-nitroquinolines **18d**,**e** can produce four different products with dimethylamine, from substitution of one chlorine atom (compounds **22**, **23**), from substitution of two chlorine atoms (compound **24**), as well as from substitution of both chlorine atoms and the methoxy group (compound **25**) (Scheme 5, Table 2). 2,4-Dichloro-6-methoxy-5-nitroquinoline (**18d**) forms only two of four possible substitution products. It completely reacted with an alcohol solution of dimethylamine over 6 days at room temperature (Table 2, experiment 1), giving a mixture of 2,4-bis(dimethylamino)quinoline **24a** and 4-chloro-2-dimethylaminoquinoline **23a**. The product resulting from substitution of one chlorine atom was identified as structure **23a**, not **22a**, based on the chemical shift of dimethylamino group signal (3.15 ppm), which is usually located at a relatively downfield position in the case of 2-dimethylamino group, compared to 4-dimethylamino group (3.23–3.24 ppm for 2-dimethylaminoquinoline,[20,21] 3.23 ppm for compound **23b**, 3.05 ppm for 4-dimethylaminoquinoline,[22] 2.86 ppm for compound **22b**). Increasing the reaction temperature (Table 2, experiment 2) shifted the product ratio in favor of bis(dimethylamino) derivative **24a**, but did not produce even a trace of the trisubstituted product **25a**. 2,4-Dichloro-8-methoxyquinoline (**18e**) completely reacted with dimethylamine in alcohol solution at room temperature over 3 days but formed a mixture of monosubstituted products **22b** (major component) and **23b** (minor component) in this case (Table 2, experiment 3). This observation confirmed

Scheme 4

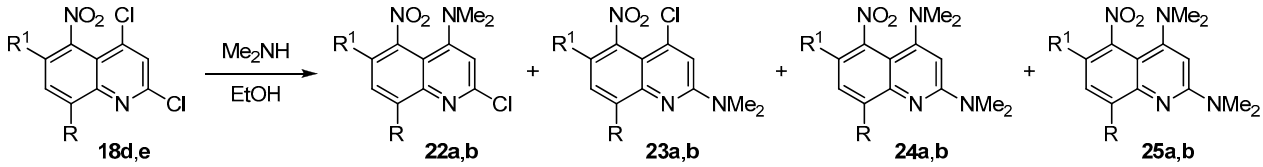


18, **20** **a** R = H, R^1 = OMe, **b** R = OMe, R^1 = H; **21a** R = H, R^1 = NMe_2, **b** R = NMe_2, R^1 = H

Table 1. The reaction of 4-chloro-2-methyl-5-nitroquinolines **18a**,**b** with dimethylamine

Experiment	Starting compound	Reaction conditions	Yield, %	
			20	**21**
1	**18a**	–15°C, 20 days	No reaction	
2		5°C, 20 days	Trace	–
3		rt, 14 days	–	30
4		120–125°C, sealed ampoule, 3 h	–	3
5	**18b**	rt, 20 days	37	18
6		125–130°C, sealed ampoule, 7 h	–	38

Scheme 5



22–24 a R = H, R^1 = OMe, **b** R = OMe, R^1 = H; **25 a** R = H, R^1 = NMe_2, **b** R = NMe_2, R^1 = H

Table 2. The reaction of 2,4-dichloro-5-nitroquinolines **18d**,**e** with dimethylamine

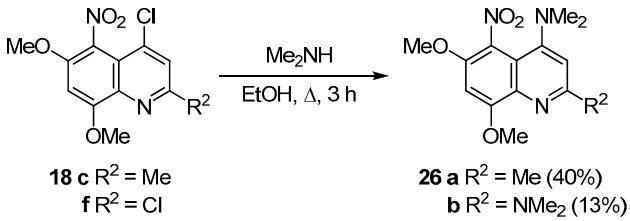
Experiment	Starting compound	Reaction conditions	Yield, %			
			22	**23**	**24**	**25**
1	**18d**	rt., 6 days	–	44	32	–
2		90–95°C, scaled ampoule, 4 h	–	20	68	–
3	**18e**	rt, 3 days	64	10	–	–
4		70–80 °C, sealed ampoule, 1 h	Mixture of compounds **22**–**25 b**			
5		110–120 °C, sealed ampoule, 3 h	Trace	Trace	46	Trace
6		140–145 °C, sealed ampoule, 2 h	–	–	30	30
7		140–145 °C, sealed ampoule, 7 h	–	–	11	57

an earlier report by Italian chemists[23] about the relatively higher mobility of chlorine atom at position 4 in the amino-dechlorination reaction of 2,4-dichloroquinoline. An increase of reaction mixture temperature led to bis- and tris-(dimethylamino)quinolines **24b** and **25b**.

Maintaining the 6,8-dimethoxy derivatives **18c**,**f** with dimethylamine in alcohol at room temperature did not produce complete conversion even after one month. TLC analysis in this case indicated the formation of a mixture containing at least six compounds, including the starting materials. Both reactions were complete in 3 h with heating, giving the 4-(dimethylamino) derivative **26a** (40%) and 2,4-bis(dimethylamino) derivative **26b** (13%), respectively (Scheme 6).

We were able to convert the obtained 6-methoxy-2,4-bis(dimethylamino)-5-nitroquinoline (**24a**) in two steps to the target 2,4,5-tris(dimethylamino)-6-methoxyquinoline (**10b**), the first representative of methoxy derivatives of quinoline proton sponges (Scheme 7). The nitro derivative **24a** was first reduced with iron in aqueous butanol in the presence of catalytic amount of acetic acid, giving the amine **27**. The subsequent methylation of amine **27** with excess dimethylsulfate in methanol in the presence of sodium carbonate led to the formation of

Scheme 6



18 c R^2 = Me
f R^2 = Cl

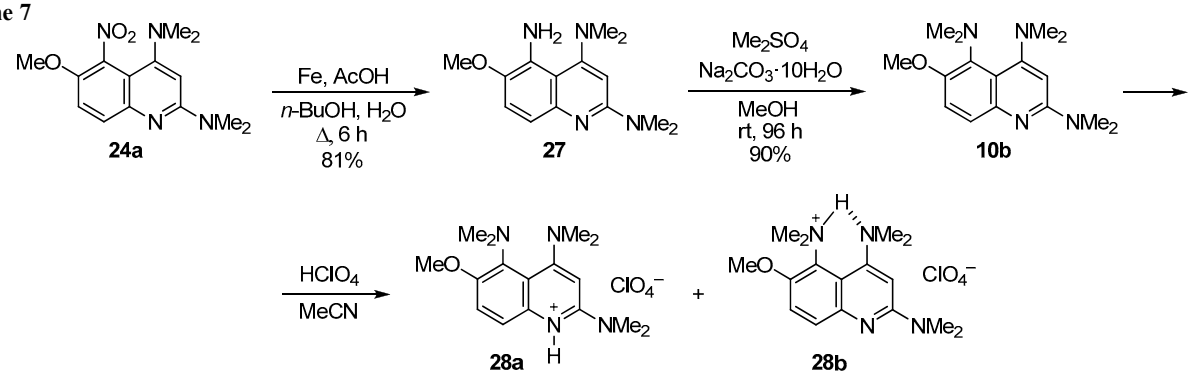
26 a R^2 = Me (40%)
b R^2 = NMe_2 (13%)

compound **10b**. The ^{1}H NMR spectrum of compound **10b** contained three singlets at 2.80, 2.88, and 3.11 ppm, corresponding to the 4-, 5-, and 2-NMe_2 groups (Fig. 1).

The attempts at obtaining compounds **11** and **12** from the respective nitro derivatives **21** and **26** by analogous procedure were not successful.

The basicity of compound **10b** determined by competitive method[24,25] in acetonitrile (pK_a 18.8) was somewhat higher than that of the original proton sponge, compound **4a**. The reaction of a slight excess of triamine **10b** with perchloric acid gave its monoperchlorate **28**. According to ^{1}H NMR data, this salt existed in CD_3CN solution as a pair of cations **28a** and **28b** with a significant prevalence of the latter (13:87). The proton chelated by *peri*-dimethylamino groups (form **28b**) gave an NMR signal at 17.98 ppm, while the

Scheme 7



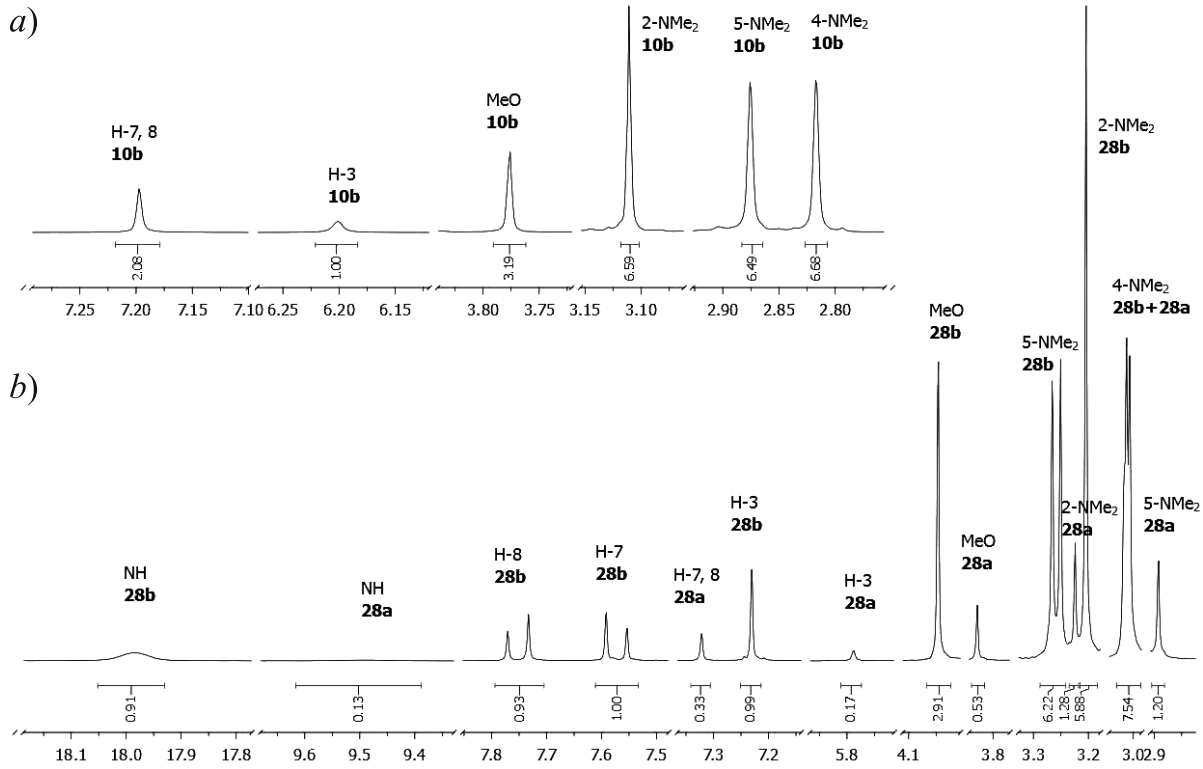


Figure 1. The ^{1}H NMR spectra (CD_3CN): *a*) free base **10b**, *b*) salt **28**.

proton at heterocycle nitrogen atom (form **28a**) gave a signal at 9.49 ppm (Fig. 1).

Thus, we have developed methods for preparing a range of 4-dimethylamino-5-nitroquinoline methoxy derivatives – necessary precursors in the synthesis of 4,5-bis(dimethylamino)quinoline methoxy derivatives, and synthesized 2,4,5-tris(dimethylamino)-6-methoxyquinoline – the first representative of such compounds. As expected, the introduction of even a single methoxy group at the *ortho* position relative to the dimethylamino groups of quinoline proton sponges resulted in stronger basicity and a substantial shift of equilibrium in their salts towards the form with proton chelated by *peri*-dimethylamino groups. 6-Methoxy-2,4,5-tris(dimethylamino)quinoline apparently is the strongest base among all currently known quinoline derivatives.

Experimental

IR spectra were recorded on an FSM-1202 instrument in vaseline oil. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-250 spectrometer (250 and 63 MHz, respectively) in CD_3CN (compounds **10b**, **28**) and in $CDCl_3$ (the rest of the compounds), with TMS as internal standard. Mass spectra (EI, 70 eV) were recorded on a Finnigan MAT INCOS 50 spectrometer. Elemental analysis was performed by the Pregl–Dumas combustion method. Melting points were determined in glass capillaries on an SMP-30 instrument. The reaction progress and purity of the obtained products was controlled by TLC on alumina plates (activity grade IV according to Brockmann) or on aluminum foil backed Sorbfil silica gel plates (TU 26-11-17-89), eluent $CHCl_3$.

Preparation of 4-chloro-2-methylquinoline methoxy derivatives 14a–c (General method). A mixture of methoxyaniline **13a–c** (40 mmol) and acetoacetic ester (5.39 ml, 42 mmol) was maintained at room temperature with periodic stirring for 14 days. The reaction mixture was separated from the water that formed, and added in several portions to refluxing Ph_2O (50 ml). Refluxing was continued for 30 min. The obtained precipitate of quinolone **16a–c** was filtered off, washed with hexane, and dried. Compounds **16a–c** were used in the next stage without additional purification.

The obtained quinolone **16a–c** was suspended in freshly distilled $POCl_3$ (20 ml, 214 mmol) and refluxed for 15 h. The reaction mixture was cooled and poured in several portions on ice, then neutralized with 10% NaOH solution. The precipitate formed was filtered off, washed with ice water, and dried, then dissolved in minimum amount of 1:1 $CHCl_3$–benzene mixture and separated by chromatography on alumina column, collecting the fraction with R_f 0.9. The solvent was removed by distillation, giving compounds **14a–c**.

4-Chloro-6-methoxy-2-methylquinoline (14a). Yield 1.87 g (23%), colorless crystals, mp 98–100°C (octane) (mp 96–98°C)[13]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.64 (3H, s, 2-CH_3); 3.91 (3H, s, OCH_3); 7.28–7.39 (3H, m, H-3,5,7); 7.88 (1H, dd, ^3J = 7.9, ^4J = 1.7, H-8). ^{13}C NMR spectrum, δ, ppm: 25.2; 56.0; 102.2; 122.5; 123.4; 126.4; 130.9; 141.5; 145.1; 156.4; 158.5. Mass spectrum, *m/z* (I_{rel}, %): 209 $[M(^{37}Cl)]^+$ (38), 207 $[M(^{35}Cl)]^+$ (100), 192 $[M(^{35}Cl)–CH_3]^+$ (42),

164 $[M(^{35}Cl)–CH_3–CO]^+$ (61). Found, %: C 63.60; H 4.84; Cl 17.09; N 6.76. $C_{11}H_{10}ClNO$. Calculated, %: C 63.62; H 4.85; Cl 17.07; N 6.74.

4-Chloro-8-methoxy-2-methylquinoline (14b). Yield 2.28 g (27%), beige crystals, mp 78–80°C (octane) (mp 80–82°C)[26]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.73 (3H, s, 2-CH_3); 4.04 (3H, s, OCH_3); 7.04 (1H, d, ^3J = 7.7, H-7); 7.38 (1H, s, H-3); 7.44 (1H, t, ^3J = 8.1, H-6); 7.71 (1H, dd, ^3J = 8.5, ^4J = 0.9, H-5). ^{13}C NMR spectrum, δ, ppm: 25.9; 56.6; 108.9; 116.1; 123.1; 126.2; 127.1; 140.9; 142.9; 155.3; 158.2. Mass spectrum, *m*/*z* (I_{rel}, %): 209 $[M(^{37}Cl)]^+$ (24), 207 $[M(^{35}Cl)]^+$ (73), 206 $[M(^{35}Cl)–H]^+$ (100), 178 $[M(^{35}Cl)–HCO]^+$ (96), 177 $[M(^{35}Cl)–CH_2O]^+$ (98). Found, %: C 63.61; H 4.83; Cl 17.09; N 6.75. $C_{11}H_{10}ClNO$. Calculated, %: C 63.62; H 4.85; Cl 17.07; N 6.74.

4-Chloro-6,8-dimethoxy-2-methylquinoline (14c). Yield 2.95 g (31%), colorless crystals, mp 139–141°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.68 (3H, s, 2-CH_3); 3.90 (3H, s, 6-OCH_3); 4.00 (3H, s, 8-OCH_3); 6.69 (1H, d, ^3J = 2.5, H-5(7)); 6.95 (1H, d, ^3J = 2.5, H-7(5)); 7.35 (1H, s, H-3). ^{13}C NMR spectrum, δ, ppm: 25.5; 55.9; 56.7; 93.9; 102.3; 123.3; 126.8; 137.7; 141.5; 155.4; 156.4; 158.8. Mass spectrum, *m*/*z* (I_{rel}, %): 239 $[M(^{37}Cl)]^+$ (29), 237 $[M(^{35}Cl)]^+$ (90), 236 $[M(^{35}Cl)–H]^+$ (100). Found, %: C 60.65; H 5.10; Cl 14.94; N 5.88. $C_{12}H_{12}ClNO_2$. Calculated, %: C 60.64; H 5.09; Cl 14.92; N 5.89.

Preparation of 2,4-dichloroquinoline methoxy derivatives 14d–f (General method). A mixture of methoxyaniline **13a–c** (61 mmol) and malonic acid (6.99 g, 67 mmol) was stirred for 40 min at 50–60°C. Freshly distilled $POCl_3$ (50 ml, 546 mmol) was added, and the mixture was refluxed for 15 h. After cooling, the reaction mixture was poured in several portions on ice, neutralized with 10% NaOH solution, and extracted with $CHCl_3$ (2×50 ml). The solvent was removed by distillation, the residue was dissolved in minimum amount of benzene and separated by chromatography on alumina column, collecting the fraction with R_f 0.8. The solvent was removed by distillation, giving compounds **14d–f**.

2,4-Dichloro-6-methoxyquinoline (14d). Yield 4.45 g (32%), pale-yellow crystals, mp 172–173°C (decomp.; 10:1 octane–benzene) (mp 170.5–171.5°C)[27]. The spectral characteristics of compound **14d** matched those described in the literature[27].

2,4-Dichloro-8-methoxyquinoline (14e). Yield 6.95 g (50%), colorless crystals, mp 136–137°C (octane) (mp 127.5–128.5°C)[28]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.02 (3H, s, OCH_3); 7.09 (1H, dd, ^3J = 7.9, ^4J = 1.0, H-7(5)); 7.47–7.54 (2H, m, H-3,6); 7.68 (1H, dd, ^3J = 8.5, ^4J = 1.1, H-5(7)). ^{13}C NMR spectrum, δ, ppm: 56.7; 110.2; 115.9; 116.0; 123.1; 128.5; 140.3; 144.7; 149.3; 155.2. Mass spectrum, *m*/*z* (I_{rel}, %): 231 $[M(^{37}Cl)]^+$ (3), 229 $[M(^{37}Cl,^{35}Cl)]^+$ (45), 227 $[M(^{35}Cl)]^+$ (75), 226 $[M(^{35}Cl)–H]^+$ (92), 198 (100), 162 (86). Found, %: C 52.63; H 3.10; Cl.08; N 6.12. $C_{10}H_7Cl_2NO$. Calculated, %: C 52.66; H3.09; Cl 31.09; N 6.14.

***N*,*N*'-bis-(2-methoxyphenyl)malonodiamide** (**17**) was isolated from the second fraction with R_f 0.3. Yield 0.48 g (5%), large, pale-yellow needles, mp 163–165°C (EtOH). IR spectrum (KBr), ν, cm^{-1}: 3319 (N–H), 1667 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.55 (2H, s, CH_2); 3.87 (6H, s, 2OCH_3); 6.86 (2H, dd, ^3J = 8.0, ^4J = 1.4, H Ar); 6.94 (2H, td, ^3J = 7.7, ^4J = 1.4, H Ar); 7.05 (2H, td, ^3J = 7.9, ^4J = 1.7, H Ar); 8.33 (2H, dd, ^3J=7.9, ^4J = 1.6, H Ar); 8.99 (2H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 46.1; 56.2; 110.6; 120.7; 121.3; 124.8; 127.6; 148.9; 165.4. Mass spectrum, *m*/*z* (I_{rel}, %): 314 $[M]^+$ (75), 123 (98), 108 (100). Found, %: C 64.94; H 5.78; N 8.92. $C_{17}H_{18}N_2O_4$. Calculated, %: C 64.96; H 5.77; N 8.91.

2,4-Dichloro-6,8-dimethoxyquinoline (14f). Yield 2.08 g (12%), pale-yellow crystals, mp 186–187°C (benzene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.83 (3H, s, 6-OCH_3); 3.91 (3H, s, 8-OCH_3); 6.62 (1H, d, ^3J = 2.5, H-7); 6.81 (1H, d, ^3J = 2.5, H-5); 7.36 (1H, s, H-3). ^{13}C NMR spectrum, δ, ppm: 55.8; 56.4; 93.7; 103.0; 122.9; 127.1; 136.6; 142.7; 146.1; 155.9; 159.5. Mass spectrum, *m*/*z* (I_{rel}, %): 261 $[M(^{37}Cl)]^+$ (8), 259 $[M(^{37}Cl,^{35}Cl)]^+$ (48), 257 $[M(^{35}Cl)]^+$ (75), 228 $[M(^{35}Cl)–HCO]^+$ (100). Found, %: C 51.20; H 3.50; Cl 27.48; N 5.44. $C_{11}H_9Cl_2NO_2$. Calculated, %: C 51.19; H 3.51; Cl 27.47; N 5.43.

Nitration of 4-chloro-2-methylquinoline and 2,4-dichloroquinoline methoxy derivatives 14a–f (General method). A solution of compound **14a–f** (7.6 mmol) in conc. H_2SO_4 (5 ml) at 0–5°C was treated by portionwise addition of nitrating mixture prepared from fuming HNO_3 (0.35 ml, 8.4 mmol) and conc. H_2SO_4 (0.70 ml, 16.0 mmol), while maintaining the temperature at or below 0–5°C. The reaction mixture was maintained at 5°C for 12 h, poured on ice (30 g), the precipitate formed was filtered off and purified by chromatography on alumina column (eluent $CHCl_3$), collecting the fractions with R_f 0.8–0.9. Removal of solvent by distillation yielded compounds **18a–f**.

4-Chloro-6-methoxy-2-methyl-5-nitroquinoline (18a). Yield 0.91 g (47%), beige crystals, mp 109–111°C (decomp., octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.67 (3H, s, 2-CH_3); 4.02 (3H, s, OCH_3); 7.43 (1H, s, H-3); 7.56 (1H, d, ^3J = 9.4, H-7); 8.14 (1H, d, ^3J = 9.4, H-8). ^{13}C NMR spectrum, δ, ppm: 25.1; 57.7; 117.2; 126.3; 133.4; 133.9; 134.2; 137.3; 143.9; 150.1; 158.3. Mass spectrum, *m*/*z* (I_{rel}, %): 254 $[M(^{37}Cl)]^+$ (35), 252 $[M(^{35}Cl)]^+$ (100), 217 $[M–Cl]^+$ (96). Found, %: C 52.26; H 3.60; Cl 14.04; N 11.07. $C_{11}H_9ClN_2O_3$. Calculated, %: C 52.29; H 3.59; Cl 14.03; N 11.09.

4-Chloro-8-methoxy-2-methyl-5-nitroquinoline (18b). The crude product was purified by silica gel column chromatography (eluent $CHCl_3$), collecting the fraction with R_f 0.4, and the solvent was evaporated. Yield 1.23 g (64%), beige crystals, mp 106–107°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.77 (3H, s, 2-CH_3); 4.12 (3H, s, OCH_3); 6.99 (1H, d, ^3J = 8.6, H-7); 7.54 (1H, s, H-3); 7.76 (1H, d, ^3J = 8.6, H-6). ^{13}C NMR spectrum, δ, ppm: 25.6; 57.4; 106.4; 118.5; 124.6; 126.8; 139.8; 140.5; 141.2; 158.2; 159.9. Mass spectrum, *m*/*z* (I_{rel}, %): 254 $[M(^{37}Cl)]^+$ (6), 252 $[M(^{35}Cl)]^+$ (18), 217 $[M–Cl]^+$ (88), 187 (100). Found, %: C 52.27; H 3.60; Cl 14.05; N 11.07. $C_{11}H_9ClN_2O_3$. Calculated, %: C 52.29; H 3.59; Cl 14.03; N 11.09.

The fraction with R_f 0.6 contained **4-chloro-8-methoxy-2-methyl-5,7-dinitroquinoline** (**19**). Yield 0.113 g (5%),

bright-yellow crystals, mp 97–99°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.80 (3H, s, 2-CH_3); 4.42 (3H, s, OCH_3); 7.63 (1H, s, H-3); 8.11 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 25.3; 65.2; 117.9; 119.9; 127.8; 139.7; 140.2; 141.2; 144.7; 153.0; 161.3. Mass spectrum, *m/z* (I_{rel}, %): 299 $[M(^{37}Cl)]^+$ (1), 297 $[M(^{35}Cl)]^+$ (3), 267 $[M(^{35}Cl)–CH_2O]^+$ (100). Found, %: C 44.37; H 2.72; Cl 11.90; N 14.11. $C_{11}H_8ClN_3O_5$. Calculated, %: C 44.39; H 2.71; Cl 11.91; N 14.12.

4-Chloro-6,8-dimethoxy-2-methyl-5-nitroquinoline (18c). Yield 0.79 g (37%), pale-yellow crystals, mp 179–181°C (benzene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, 2-CH_3); 4.01 (3H, s, 8-OCH_3); 4.11 (3H, s, 6-OCH_3); 6.82 (1H, s, H-7); 7.45 (1H, s, H-3). ^{13}C NMR spectrum, δ, ppm: 24.9; 56.9; 57.2; 95.9; 118.0; 126.7; 135.5; 137.3; 150.7; 156.7; 157.6. Found, %: C 50.97; H 3.94; Cl 12.53; N 9.90. $C_{12}H_{11}ClN_2O_4$. Calculated, %: C 50.99; H 3.92; Cl 12.54; N 9.91.

2,4-Dichloro-6-methoxy-5-nitroquinoline (18d). Yield 1.80 g (87%), Gray-green crystals, mp 157–159°C (decomp., EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.02 (3H, s, OCH_3); 7.51 (1H, s, H-3); 7.60 (1H, d, ^3J = 9.5, H-7); 8.08 (1H, d, ^3J = 9.4, H-8). ^{13}C NMR spectrum, δ, ppm: 57.3; 117.3; 117.9; 125.7; 132.9; 133.7; 138.8; 142.6; 148.8; 150.5. Mass spectrum, *m/z* (I_{rel}, %): 276 $[M(^{37}Cl)]^+$ (9), 274 $[M(^{37}Cl,^{35}Cl)]^+$ (62), 272 $[M(^{35}Cl)]^+$ (97), 237 $[M–Cl]^+$ (100). Found, %: C 43.96; H 2.22; Cl 25.95; N 10.27. $C_{10}H_6Cl_2N_2O_3$. Calculated, %: C 43.98; H 2.21; Cl 25.97; N 10.26.

2,4-Dichloro-8-methoxy-5-nitroquinoline (18e). Yield 1.22 g (59%), beige crystals, mp 153–154°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.12 (3H, s, OCH_3); 7.07 (1H, d, ^3J = 8.6, H-7); 7.66 (1H, s, H-3); 7.83 (1H, d, ^3J = 8.6, H-6). ^{13}C NMR spectrum, δ, ppm: 57.4; 107.7; 119.0; 125.7; 126.9; 140.2; 140.5; 141.7; 151.1; 157.9. Mass spectrum, *m/z* (I_{rel}, %): 274 $[M(^{37}Cl,^{35}Cl)]^+$ (1), 272 $[M(^{35}Cl)]^+$ (3), 207 (38), 30 $[CH_2O]^+$ (100). Found, %: C 43.96; H 2.20; Cl 25.94; N 10.28. $C_{10}H_6Cl_2N_2O_3$. Calculated, %: C 43.98; H 2.21; Cl 25.97; N 10.26.

2,4-Dichloro-6,8-dimethoxy-5-nitroquinoline (18f). Yield 0.99 g (43%), beige crystals, mp 238–239°C (*n*-BuOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.04 (3H, s, 8-OCH_3); 4.12 (3H, s, 6-OCH_3); 6.87 (1H, s, H-7); 7.58 (1H, s, H-3). ^{13}C NMR spectrum, δ, ppm: 56.9; 57.3; 96.8; 118.6; 126.6; 127.6; 134.7; 139.2; 147.8; 151.8; 157.5. Found, %: C 43.57; H 2.65; Cl 23.41; N 9.23. $C_{11}H_8Cl_2N_2O_4$. Calculated, %: C 43.59; H 2.66; Cl 23.39; N 9.24.

Reaction of 4-chloro-5-nitroquinoline methoxy derivatives 18a–f with dimethylamine (General method).

A. A solution or suspension of compound **18a–f** (1 mmol) and liquid Me_2NH (1 ml, 15 mmol) in EtOH (5 ml) was maintained at room temperature for 3–20 days. The reaction mixture was evaporated, the residue was separated by silica gel column chromatography with $CHCl_3$ as eluent.

B. A mixture of compound **18a–f** (1 mmol), EtOH (3 ml), and liquid Me_2NH (1 ml, 15 mmol) was sealed in an ampoule. The ampoule was placed in a safety vessel and maintained for 2–7 h at 80–145°C, then cooled and opened. The reaction mixture was evaporated, the residue was separated by silica gel column chromatography with $CHCl_3$ as eluent.

The following methods provided the optimum yields of reaction products.

Compound **18a** (253 mg, 1 mmol) gave ***N*^{4},*N*^{4},*N*^{6},*N*^{6},2-pentamethyl-5-nitroquinoline-4,6-diamine (21a)** (fraction with R_f 0.4) after maintaining the reaction mixture for 14 days according to method A. Yield 83 mg (30%).

Compound **18b** (253 mg, 1 mmol) gave ***N*^{4},*N*^{4},*N*^{8},*N*^{8},2-pentamethyl-5-nitroquinoline-4,8-diamine (21b)** (fraction with R_f 0.4, yield 50 mg (19%)) and **8-methoxy-*N*,*N*,2-trimethyl-5-nitroquinoline-4-amine (20b)** (fraction with R_f 0.2, yield 97 mg (39%)) after maintaining the reaction mixture for 20 days according to method A.

Compound **18b** (252 mg, 1 mmol) gave compound **21b** (fraction with R_f 0.4) after heating the reaction mixture for 7 h at 125–130°C according to method B. Yield 104 g (38%).

Compound **18c** (283 mg, 1 mmol) gave **6,8-dimethoxy-*N*,*N*,2-trimethyl-5-nitroquinoline-4-amine (26a)** (fraction with R_f 0.3) after heating the reaction mixture at 80–85°C for 3 h according to method B. Yield 116 mg (40%).

Compound **18d** (546 mg, 2 mmol) gave **4-chloro-6-methoxy-*N*,*N*-dimethyl-5-nitroquinoline-2-amine (23a)** (fraction with R_f 0.4, yield 248 mg (44%)) and **6-methoxy-*N*^{2},*N*^{2},*N*^{4},*N*^{4}-tetramethyl-5-nitroquinoline-2,4-diamine (24a)** (fraction with R_f 0.2, yield 186 mg (32%)) after maintaining the reaction mixture for 6 days according to method A.

Compound **18e** (118 mg, 0.43 mmol) gave **4-chloro-8-methoxy-*N*,*N*-dimethyl-5-nitroquinoline-2-amine (23b)** (fraction with R_f 0.3, yield 12 mg (10%)) and **2-chloro-8-methoxy-*N*,*N*-dimethyl-5-nitroquinoline-4-amine (22b)** (fraction with R_f 0.2, yield 78 mg (64%)) after maintaining the reaction mixture for 3 days according to method A.

Compound **18e** (164 mg, 0.6 mmol) gave **8-methoxy-*N*^{2},*N*^{2},*N*^{4},*N*^{4}-tetramethyl-5-nitroquinoline-2,4-diamine (24b)** (fraction with R_f 0.5) after maintaining the reaction mixture at 110–120°C for 3 h according to method B. Yield 79 mg (46%).

Compound **18e** (103 mg, 0.38 mmol) gave compound **24b** (fraction with R_f 0.5, yield 12 mg (11%)) and ***N*^{2},*N*^{2},*N*^{4},*N*^{4},*N*^{8},*N*^{8}-hexamethyl-5-nitroquinoline-2,4,8-triamine (25b)** (fraction with R_f 0.4, yield 66 mg (57%)) after heating the reaction mixture at 140–145°C for 7 h according to method B.

Compound **18f** (300 mg, 1 mmol) gave **6,8-dimethoxy-*N*^{2},*N*^{2},*N*^{4},*N*^{4}-tetramethyl-5-nitroquinoline-2,4-diamine (26b)** (fraction with R_f 0.4) after heating the reaction mixture at 140–145°C for 3 h according to method B. Yield 42 mg (13%).

Compound 20b. Orange crystals, mp 163–164°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.69 (3H, s, 2-CH_3); 2.83 (6H, s, $N(CH_3)_2$); 4.09 (3H, s, OCH_3); 6.82 (1H, s, H-3); 6.89 (1H, d, ^3J = 8.5, H-7); 7.79 (1H, d, ^3J = 8.5, H-6). ^{13}C NMR spectrum, δ, ppm: 25.7; 42.7; 56.7; 104.6; 110.6; 113.3; 122.7; 141.8; 142.0; 155.3; 158.5; 159.5. Mass spectrum, *m/z* (I_{rel}, %): 261 $[M]^+$ (61), 215 $[M–NO_2]^+$ (100). Found, %:

C 59.74; H 5.78; N 16.10. $C_{13}H_{15}N_3O_3$. Calculated, %: C 59.76; H 5.79; N 16.08.

Compound 21a. Beige crystals, mp 127–128°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.64 (3H, s, 2-CH_3); 2.65 (6H, s, 4-N(CH_3)$_2$); 2.78 (6H, s, 6-N(CH_3)$_2$); 6.98 (1H, s, H-3); 7.61 (1H, d, ^3J = 9.1, H-7); 8.01 (1H, d, ^3J = 9.1, H-8). ^{13}C NMR spectrum, δ, ppm: 25.6; 45.6; 45.9; 114.9; 116.6; 124.2; 132.1; 142.5; 144.3; 147.2; 157.8; 159.9. Mass spectrum, *m*/*z* (I_{rel}, %): 274 $[M]^+$ (50), 228 $[M–NO_2]^+$ (54), 185 (100). Found, %: C 61.34; H 6.60; N 20.40. $C_{14}H_{18}N_4O_2$. Calculated, %: C 61.30; H 6.61; N 20.42.

Compound 21b. Red crystals, mp 136–137°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.63 (3H, s, 2-CH_3); 2.82 (6H, s, 4-N(CH_3)$_2$); 3.18 (6H, s, 8-N(CH_3)$_2$); 6.72–6.75 (2H, m, H-3,7); 7.74 (1H, d, ^3J = 8.5, H-6). ^{13}C NMR spectrum, δ, ppm: 25.4; 42.4; 44.1; 109.2; 110.3; 113.6; 123.3; 140.6; 143.4; 153.7; 155.2; 156.5. Found, %: C 61.33; H 6.59; N 20.41. $C_{14}H_{18}N_4O_2$. Calculated, %: C 61.30; H 6.61; N 20.42.

Compound 22b. Orange crystals, mp 134–135°C (benzene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.86 (6H, s, N(CH_3)$_2$); 4.05 (3H, s, OCH_3); 6.84 (1H, s, H-3); 6.88 (1H, d, ^3J = 8.6, H-7); 7.87 (1H, d, ^3J = 8.6, H-6). ^{13}C NMR spectrum, δ, ppm: 42.8; 57.1; 106.0; 109.9; 113.7; 124.4; 141.9; 152.4; 156.9; 158.9. Mass spectrum, *m*/*z* (I_{rel}, %): 283 $[M(^{37}Cl)]^+$ (30), 281 $[M(^{35}Cl)]^+$ (85), 235 $[M(^{35}Cl)–NO_2]^+$ (100). Found, %: C 51.17; H 4.28; Cl 12.58; N 14.93. $C_{12}H_{12}ClN_3O_3$. Calculated, %: C 51.17; H 4.29; Cl 12.59; N 14.92.

Compound 23a. Yellow needles, mp 173–174°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.15 (6H, s, N(CH_3)$_2$); 3.93 (3H, s, OCH_3); 6.99 (1H, s, H-3); 7.36 (1H, d, ^3J = 9.4, H-7); 7.76 (1H, d, ^3J = 9.4, H-8). ^{13}C NMR spectrum, δ, ppm: 37.8; 57.4; 111.9; 112.7; 117.0; 130.3; 134.7; 137.2; 144.2; 146.3; 156.1. Mass spectrum, *m*/*z* (I_{rel}, %): 283 $[M(^{37}Cl)]^+$ (35), 281 $[M(^{35}Cl)]^+$ (100), 252 $[M(^{35}Cl)–HCO]^+$ (31). Found, %: C 51.18; H 4.28; Cl 12.60; N 14.90. $C_{12}H_{12}ClN_3O_3$. Calculated, %: C 51.17; H 4.29; Cl 12.59; N 14.92.

Compound 23b. Yellowish-orange crystals, mp 134–135°C (isooctane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.23 (6H, s, N(CH_3)$_2$); 4.03 (3H, s, OCH_3); 6.83 (1H, d, ^3J= 8.5, H-7); 7.03 (1H, s, H-3); 7.43 (1H, d, ^3J=8.5, H-6). ^{13}C NMR spectrum, δ, ppm: 38.1; 57.1; 106.6; 112.7; 113.5; 119.8; 139.9; 141.2; 141.7; 156.7; 157.2. Mass spectrum, *m*/*z* (I_{rel}, %): 283 $[M(^{37}Cl)]^+$ (32), 281 $[M(^{35}Cl)]^+$ (100), 252 $[M(^{35}Cl)–HCO]^+$ (33). Found, %: C 51.17; H 4.27; Cl 12.57; N 14.94. $C_{12}H_{12}ClN_3O_3$. Calculated, %: C 51.17; H 4.29; Cl 12.59; N 14.92.

Compound 24a. Orange needles, mp 209–211°C (benzene–octane, 2:1). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.61 (6H, s, 4-N(CH_3)$_2$); 3.15 (6H, s, 2-N(CH_3)$_2$); 3.90 (3H, s, OCH_3); 6.56 (1H, s, H-3); 7.28 (1H, d, ^3J = 9.3, H-7); 7.71 (1H, d, ^3J = 9.3, H-8). ^{13}C NMR spectrum, δ, ppm: 38.4; 45.5; 57.8; 102.4; 112.6; 116.5; 129.8; 135.9; 145.2; 146.0; 158.1; 158.3. Mass spectrum, *m*/*z* (I_{rel}, %): 290 $[M]^+$ (100), 275 $[M–CH_3]^+$ (46), 255 (75), 244 $[M–NO_2]^+$ (82). Found, %: C 57.90; H 6.26; N 19.31. $C_{14}H_{18}N_4O_3$. Calculated, %: C 57.92; H 6.25; N 19.30.

Compound 24b. Orange crystals, mp 182–183°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.75 (6H, s, 4-N(CH_3)$_2$); 3.22 (6H, s, 2-N(CH_3)$_2$); 4.02 (3H, s, OCH_3); 6.27 (1H, s, H-3); 6.75 (1H, d, ^3J = 8.4, H-7); 7.42 (1H, d, ^3J = 8.4, H-6). ^{13}C NMR spectrum, δ, ppm: 38.2; 43.5; 56.9; 97.7; 105.6; 110.5; 118.6; 142.5; 142.7; 157.2; 158.9. Mass spectrum, *m*/*z* (I_{rel}, %): 290 $[M]^+$ (100), 275 $[M–CH_3]^+$ (21), 214 (44). Found, %: C 57.94; H 6.24; N 19.32. $C_{14}H_{18}N_4O_3$. Calculated, %: C 57.92; H 6.25; N 19.30.

Compound 25b. Bright-red crystals, mp 175–176°C (octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.73 (6H, s, 4 N(CH_3)$_2$); 3.12 (6H, s, 8-N(CH_3)$_2$); 3.16 (6H, s, 2-N(CH_3)$_2$); 6.19 (1H, s, H-3); 6.65 (1H, d, ^3J = 8.4, H-7); 7.40 (1H, d, ^3J = 8.4, H-6). ^{13}C NMR spectrum, δ, ppm: 38.5; 43.3; 43.9; 96.6; 110.5; 111.6; 119.5; 142.0; 143.9; 151.7; 157.3; 157.4. Mass spectrum, *m*/*z* (I_{rel}, %): 303 $[M]^+$ (100), 288 $[M–CH_3]^+$ (72), 241 (100), 227 (48). Found, %: C 59.36; H 6.99; N 23.10. $C_{15}H_{21}N_5O_2$. Calculated, %: C 59.39; H 6.98; N 23.09.

Compound 26a. Orange crystals, mp 118–119°C (decomp., octane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.66 (6H, s, N(CH_3)$_2$); 2.69 (3H, s, 2-CH_3); 3.99 (3H, s, 8-OCH_3); 4.10 (3H, s, 6-OCH_3); 6.74 (1H, s, H-7); 7.01 (1H, s, H-3). ^{13}C NMR spectrum, δ, ppm: 25.4; 44.7; 56.6; 57.3; 95.2; 115.1; 117.2; 136.2; 143.2; 149.6; 156.8; 157.6; 157.8. Found, %: C 57.70; H 5.89; N 14.43. $C_{14}H_{17}N_3O_4$. Calculated, %: C 57.72; H 5.88; N 14.42.

Compound 26b. Brown crystals, mp 168–169°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.63 (6H, s, 4-N(CH_3)$_2$); 3.20 (6H, s, 2-N(CH_3)$_2$); 3.93 (3H, s, 6-OCH_3); 4.04 (3H, s, 8-OCH_3); 6.53 (1H, s, H-3); 6.67 (1H, s, H-7). ^{13}C NMR spectrum, δ, ppm: 37.9; 44.7; 56.6; 57.6; 96.6; 101.5; 112.6; 128.3; 146.4; 155.8; 157.3; 158.1. Found, %: C 56.26; H 6.30; N 17.47. $C_{15}H_{20}N_4O_4$. Calculated, %: C 56.24; H 6.29; N 17.49.

6-Methoxy-*N*^{2},*N*^{2},*N*^{4},*N*^{4}-tetramethylquinoline-2,4,5-triamine (27). A mixture of compound **24a** (145 mg, 0.5 mmol), iron powder (280 mg, 5.0 mmol), *n*-BuOH (3 ml), H_2O (1 ml), and 5 drops of AcOH was refluxed for 6 h. The solution was filtered while hot, then cooled. The precipitate formed was filtered off, dissolved in $CHCl_3$ (5 ml), and purified by chromatography on alumina column (eluent $CHCl_3$), collecting the fraction with R_f 0.3. Yield 105 mg (81%), yellowish-orange needles, mp 136–137°C (EtOH). IR spectrum, ν, cm^{-1}: 3353, 3466 (NH_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.75 (6H, s, 4-N(CH_3)$_2$); 3.14 (6H, s, 2-N(CH_3)$_2$); 3.87 (3H, s, OCH_3); 5.63 (1H, br. s, NH_2); 6.33 (1H, s, H-3); 7.02 (1H, d, ^3J = 8.9, H-7); 7.14 (1H, d, ^3J = 8.9, H-8). ^{13}C NMR spectrum, δ, ppm: 38.1; 45.0; 56.7; 96.4; 107.9; 113.8; 115.5; 133.1; 139.6; 145.9; 157.1; 160.5. Mass spectrum, *m*/*z* (I_{rel}, %): 260 $[M]^+$ (83), 245 $[M–CH_3]^+$ (100), 230 $[M–CH_2O]^+$ (18). Found, %: C 64.57; H 7.75; N 21.50. $C_{14}H_{20}N_4O$. Calculated, %: C 64.59; H 7.74; N 21.52.

6-Methoxy-*N*^{2},*N*^{2},*N*^{4},*N*^{4},*N*^{5},*N*^{5}-hexamethylquinoline-2,4,5-triamine (10b). A solution of compound **27** (0.041 g, 0.16 mmol) in MeOH (5 ml) was treated with Na_2CO_3·$10H_2O$ (0.450 g, 1.58 mmol) and Me_2SO_4 (0.147 ml, 1.58 mmol). The mixture was stirred at room temperature for 96 h. The

solvent was evaporated, the residue was dissolved in a minimum amount of 1:1 $CHCl_3$–acetone mixture and separated by alumina column chromatography by eluting with the same mixture and collecting the fraction with R_f 0.3. Yield 41 mg (90%), light-brown oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.80 (6H, s, 4-N(CH_3)$_2$); 2.86 (6H, s, 5-N(CH_3)$_2$); 3.13 (6H, s, 2-N(CH_3)$_2$); 3.75 (3H, s, OCH_3); 6.06 (1H, s, H-3); 7.14 (1H, d, ^3J = 9.0, H-7); 7.31 (1H, d, ^3J = 9.1, H-8). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.80 (6H, s, 4-N(CH_3)$_2$); 2.88 (6H, s, 5-N(CH_3)$_2$); 3.11 (6H, s, 2-N(CH_3)$_2$); 3.75 (3H, s, OCH_3); 6.20 (1H, s, H-3); 7.20 (2H, s, H-7,8). ^{13}C NMR spectrum, δ, ppm: 38.0; 43.7; 44.1; 58.6; 94.2; 113.6; 119.4; 121.9; 137.6; 147.5; 150.8; 157.8; 158.7. Found,%: C 66.63; H 8.40; N 19.42. $C_{16}H_{24}N_4O$. Calculated, %: C 66.64; H 8.39; N 19.43.

6-Methoxy-*N*^{2},*N*^{2},*N*^{4},*N*^{4},*N*^{5},*N*^{5}-hexamethylquinoline-2,4,5-triamine perchlorate (28). A solution of quinoline **10b** (28.0 mg, 0.097 mmol) in MeCN (1 ml) was treated with a solution of 63% $HClO_4$ (12.3 mg, 0.077 mmol, 0.8 equiv) in MeCN (1 ml). The solvent was evaporated, the excess of base **10b** was removed by extraction with Et_2O (4×2 ml). Yield 27 mg (90%), beige crystals, mp 234-237°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz) (a mixture of forms **28a** and **28b** in 13:87 ratio): 2.89 (0.78H, s, 5-N(CH_3)$_2$ (**28a**)); 3.01 (0.78H, s, 4-N(CH_3)$_2$ (**28a**)); 3.01 (5.22H, d, ^3J = 1.4, 4-N(CH_3)$_2$ (**28b**)); 3.20 (5.22H, s, 2-N(CH_3)$_2$ (**28b**)); 3.22 (0.78H, s, 2-N(CH_3)$_2$ (**28a**)); 3.26 (5.22H, d, ^3J = 3.7, 5-N(CH_3)$_2$ (**28b**)); 3.83 (0.39H, s, OCH_3 (**28a**)); 4.05 (2.61H, s, OCH_3 (**28b**)); 5.79 (0.13H, s, H-3 (**28a**)); 7.23 (0.87H, s, H-3 (**28b**)); 7.32 (0.26H, s, H-7,8 (**28a**)); 7.57 (0.87H, d, ^3J = 9.5, H-7 (**28b**)); 7.75 (0.87H, d, ^3J = 9.4, H-8 (**28b**)); 9.49 (0.13H, br. s, N^+H (**28a**)); 17.98 (0.87H, br. s, N^+H (**28b**)).

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