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SYNTHESIS OF 4,5-BIS(DIMETHYLAMINO)QUINOLINES AND THE DUAL DIRECTION OF THEIR PROTONATION

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A study on the synthesis of derivatives of 4,5-bis(dimethylamino)quinoline, which is a quinoline analog of 1,8-bis(dimethylamino)naphthalene (also known by its trade name Proton Sponge) was carried out. The first two representatives of this series were obtained. Depending on the aggregate state, solvent, and structural features, these compounds may be protonated either at the quinoline heteroatom or peri-NMe_2 groups.

Keywords: 4,5-bis(dimethylamino)quinoline, proton sponges, quinolines, basicity, proton transfer, tautomerism.

The formation and study of neutral organic superbases is an interesting and rapidly developing field in modern organic chemistry [1, 2]. The discovery of so-called proton sponges has served as an impetus for this work [3, 4]. The first proton sponge was 1,8-bis(dimethylamino)naphthalene (**1**), which has abnormally high basicity for an arylamine: pK_a = 12.1 in water [5], 7.5 in DMSO [6], and 18.62 in acetonitrile [7]. Since such basicity is due to the spatial proximity of the dimethylamino groups, which destabilizes the base, research on the creation of other superbases started using this compound as a model. For example, this approach was found to be valid for quino[7,8-*h*]quinoline (**2**) (pK_a = 12.8 in water [8, 9]) and, especially, for vinamidine **3** synthesized by Schwesinger [10] (pK_a = 31.94 in acetonitrile). However, strictly speaking, quinolines **2** and **3** are not proton sponges, since unlike the latter they are kinetically active, i.e., at a rate close to diffusion they add and donate a proton and react readily enough at the nitrogen atoms with various Lewis acids. Therefore bases **2** and **3** should be characterized as proton-sponge-like compounds [1].

In this regard, it was of interest to obtain previously unreported 4,5-bis(dimethylamino)quinoline (**4**), especially since this compound has two special features. Firstly, it is difficult to predict whether quinoline **4** would behave as a proton sponge or would undergo protonation at the ring nitrogen atom due to the strong +M-effect of the *peri*-dimethylamino groups. Secondly, quinoline **4** is very similar to 4-dimethylaminopyridine (**5**), which is known for its strong catalytic activity in a whole series of reactions, especially in transacylation [11, 12]. We could predict with high probability that quinoline proton sponge **4** would be more basic than pyridine **5** and if its protonation occurs at the heteroatom the catalytic activity of quinoline **4** would be much greater. Hence, we undertook a study to create methods for the synthesis of quinoline **4** and its derivatives.

By analogy with proton sponge **1**, 4,5-dinitroquinoline or one of the two isomeric *peri*-nitroamino-quinolines may serve as precursors for quinoline **4**. However, a problem arises, quinoline, in contrast to naphthalene, cannot be nitrated as readily at both *peri* positions and, especially at the heterocycle. Thus, we

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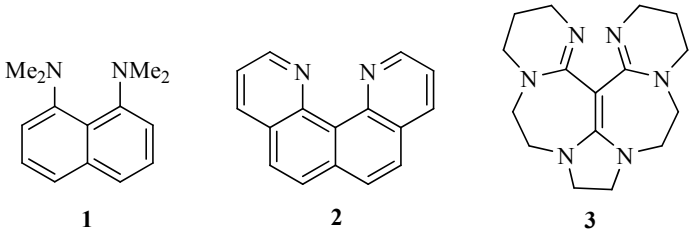
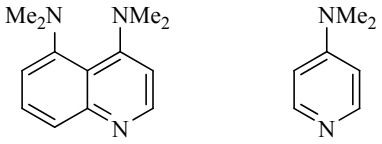
could only plan the consecutive introduction of a nitro group or dimethylamino groups (for example, through aminodehalogenation) to its *peri* positions, relying on different methods for activating the heterocycle and protecting the other terminal atoms in this ring, which compete with the atoms in the *peri* positions. Among the activation methods, we looked promising introduction of an *N*-oxide functionality into the heterocycle or inclusion of metallation steps in the synthesis scheme.



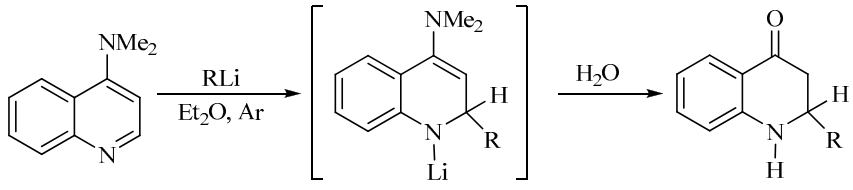
1 **2** **3**



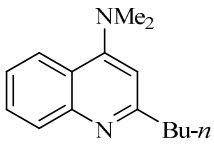
4 **5**

Metallation. Relatively easily available 4-dimethylaminoquinoline (**6**) [13] and 5-dimethylamino-quinoline (**11**), obtained by the methylation of 5-aminoquinoline (**10**), were selected as reagents for metallation. We came out of their structural similarity to 1-dimethylaminonaphthalene, which is metallated with high regioselectivity by *n*-butyllithium or *tert*-butyllithium at position 8. If quinolines **6** and **11** would undergo similar metallation, the subsequent action of electrophiles such as tosyl azide might lead us in two or three steps to the target 4,5-bis(dimethylamino)quinoline (**4**).

Although the direct metallation of the quinoline system is well known [15-23], we found that quinoline **6** adds *n*-butyllithium or *tert*-butyllithium at the C=N bond quite rapidly (over 1 h) in the temperature range from -15 to +20°C. The immediate hydrolysis of adducts **7a**,**b** gives 2-alkyl-2,3-dihydroquinolones **8a**,**b**. When the metallation reaction time is extended to 96 h, LiH is cleaved in the case of adduct **7a**, leading to 2-*n*-butyl-4-dimethylaminoquinoline (**9**) after hydrolysis. Thus, only quinolone **8a** after 1 h, or only quinoline **9** (96 h), or a mixture of these compounds (24 h) was found in the reaction mixture depending on the reaction time as indicated by ^{1}H NMR spectroscopy (Table 1). Adduct **7b** with a *tert*-butyl substituent gives only quinolone **8b** independently of the reaction time. The addition of a ligand, namely, *N,N,N',N'*-tetramethylethylidenediamine (TMEDA), does not affect the reaction course but slightly reduces the rate of elimination of LiH.



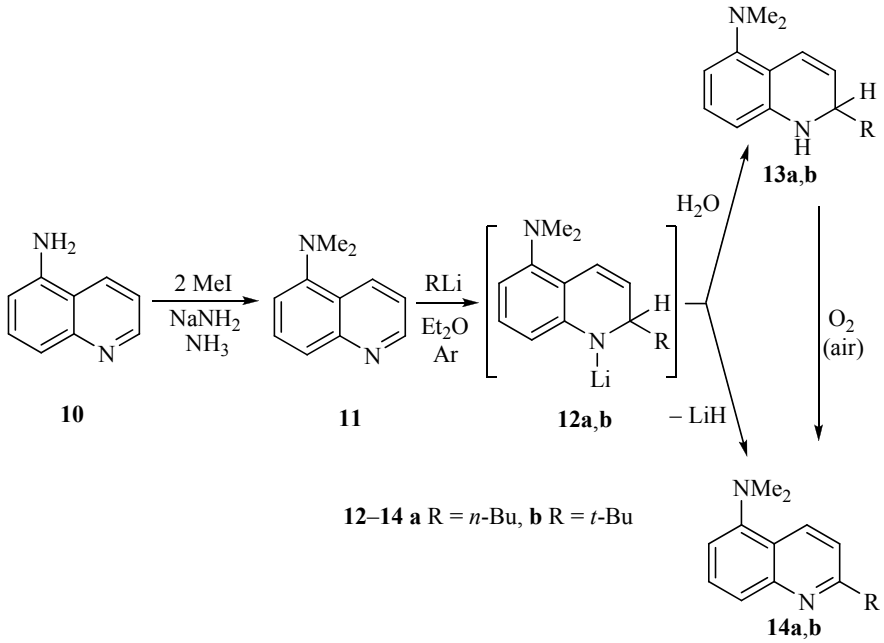
6 **7a,b** **8a,b**



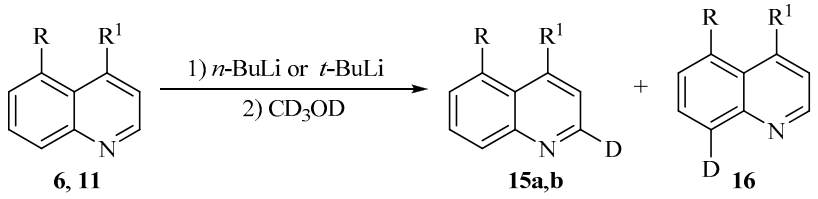
9

7, **8 a** R = *n*-Bu, **b** R = *t*-Bu

5-Dimethylaminoquinoline (**11**), similar to its isomer **6** adds alkyllithiums to the C=N bond independently of the temperature (-15°C or +20°C) and in the presence or absence of TMEDA. The ^{1}H NMR spectra of the reaction mixtures after hydrolysis show signals related to 2-alkyl-1,2-dihydro-5-dimethylaminoquinolines **13a**,**b** and 2-alkyl-5-dimethylaminoquinolines **14a**,**b** (Table 1). These products are readily separated by column chromatography but dihydro derivatives **13a**,**b** proved to be unstable and oxidized upon standing over few hours to give quinolines **14a**,**b**. Seemingly, quinolines **14a**,**b** might be formed directly from adducts **12a**,**b** by elimination of lithium hydride in the step preceding hydrolysis.



The treatment of quinolines **6** and **11** with *n*-BuLi or *t*-BuLi as metallating agents at -78°C over 1-2 h with the subsequent addition of CD_3OD lead only to the partial lithiation at position 2 and 8 in quinoline **11** (formation of deutero derivatives **15b** and **16**) and at position 2 in quinoline **6** (formation of compound **15a**). Evidence for this assumption is found in the reduction of the integral intensity by about 20% of the corresponding signals in the ^{1}H NMR spectra of the crude mixtures.



6, **15a** R = H, R^1 = NMe_2; **11**, **15b**, **16** R = NMe_2, R^1 = H

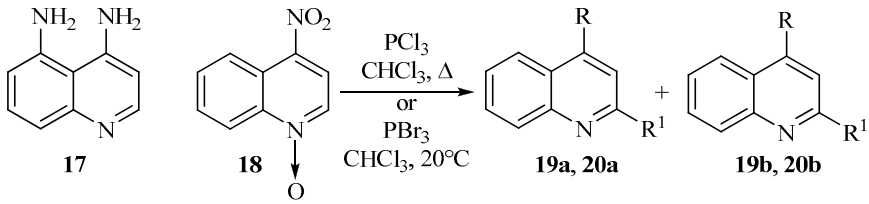
Thus, our experiments showed that quinolines **6** and **11** are not metallated at the *peri* position relative to the NMe_2 group. The lack of a directing effect may be related to a strong conjugation of the 4- and 5-dimethylamino groups with the quinoline nitrogen atom such that these groups become planar and coplanar to the ring system. On the other hand, at low temperature, electron-withdrawing and coordinating effects of the ring heteroatom begin to appear, leading to partial metallation at position 2 and/or 8.

TABLE 1. Conditions for the Metallation of Quinolines **6** and **11** and Reaction Product Yields

Compound	RLi	Reaction temperature, °C	Time, h	Yield*, %			
				8	**9**	**13**	**14**
6	*n*-BuLi	20	96	0 (9*[2])	100 (91*[2])	—	—
		20	24	50 (56*[2])	50 (37*[2])	—	—
		-15	24	50 (66*[2])	50 (33*[2])	—	—
		-15	1	100	—	—	—
	t-BuLi	-15	1	100	—	—	—
11	*n*-BuLi	20	96	—	—	100*[2]	—
		20	24	—	—	77	23
		-15	24	—	—	77	23
		-15	1	—	—	71	29
	t-BuLi	-15	24	—	—	50	50
		-15	1	—	—	75.5	15.5

*According to ^{1}H NMR spectra of the reaction mixture.
*[2]Reactions were carried out in the presence of TMEDA.

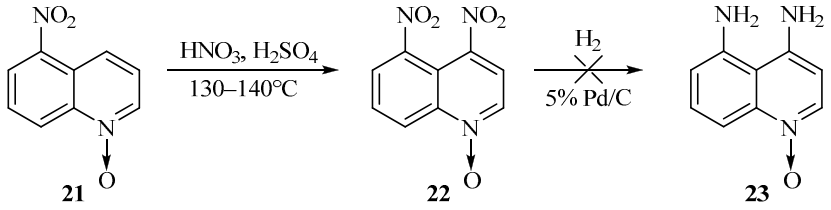
Use of 4-nitro- and 5-nitroquinoline 1-oxides. Kaneko et al. [24] have reported the synthesis of 4,5-diaminoquinoline (**17**) from 4-nitroquinoline 1-oxide (**18**) by deoxygenation of oxide **18** using phosphorus tribromide to give 4-nitroquinoline, which was then consecutively nitrated at position 5 and reduced to give diamine **17**. However, we were unable to reproduce this result due to difficulties in removing the *N*-oxide function, already noted repeatedly by other workers [25, 26]. We found that treatment of oxide **18** with phosphorus trichloride in chloroform at 60°C gives a 1:1 mixture of 4-chloro- (**19a**) and 2,4-dichloroquinolines (**19b**). As already reported by Denny et al. [25], the use of PBr_3 in chloroform at 20°C led to a mixture of predominantly 2,4-dibromo- (**20a)** along with 2-bromo-4-nitroquinoline (**20b**). At lower temperatures (from -15° to 0°C), starting *N*-oxide **18** remained unchanged.



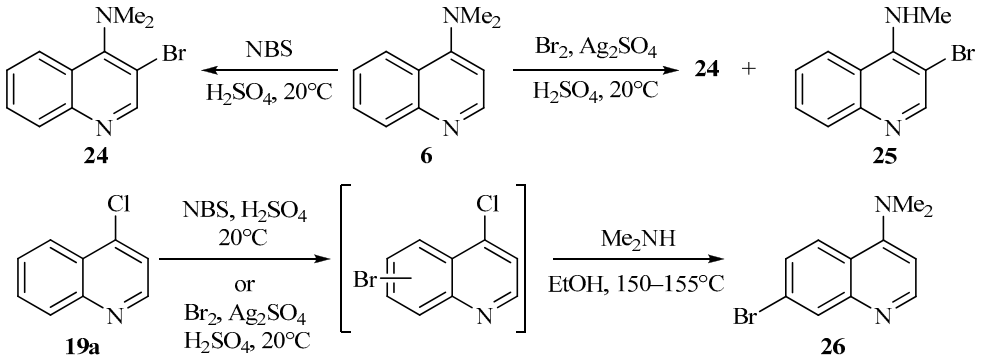
19a R = Cl, R^1 = H; **b** R = R^1 = Cl; **20 a** R = R^1 = Br; **b** R = NO_2, R^1 = Br

We also were unable to make a nitration of 4-nitroquinoline 1-oxide (**18**) since this compound was completely inert to a nitrating mixture of concentrated nitric and sulfuric acids in the temperature range from 70 to 150°C. On the other hand, 5-nitroquinoline 1-oxide (**21**) described by Ochiai [27] underwent nitration to give 4,5-dinitroquinoline 1-oxide (**22**). However, the reaction proceeded slowly (16 h) under very vigorous conditions (130-140°C) to give a yield of only 20%, while product **22** was very difficult to separate from

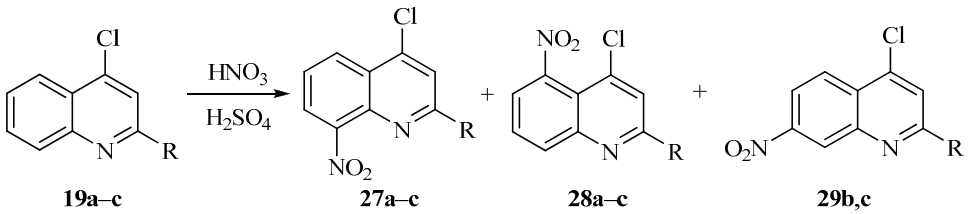
starting oxide **18** even using preparative thin-layer chromatography. A series of experiments was carried out on the reduction of quinoline **22** with hydrogen in the presence of 5% Pd/C in methanol or acetic acid. Unfortunately, these experiments were unsuccessful, and no traces of diamine **17** or its *N*-oxide **23** were detected. Apparently, under these conditions not only the nitro group but also the heterocycle itself is getting reduced. Such behavior has been reported repeatedly for quinolines [28-32] and quinoline 1-oxides [33].



Electrophilic substitution in 4-dimethylaminoquinoline and 4-chloroquinoline. We then attempted the introduction of the required substituents into the quinoline *peri* positions by bromination and nitration of 4-dimethylaminoquinoline and 4-chloroquinoline. We proceeded from the fact that bromination of unsubstituted quinoline occurred at positions 5 or 8 by bromine or bromosuccinimide (NBS) in sulfuric acid [34]. The substituents at position 4 were found to have a significant effect on the direction of the halogenation. Thus, 4-dimethylaminoquinoline (**6**) is brominated by NBS in sulfuric acid exclusively at position 3 to give bromide **24**. It is interesting that a small amount (5%) demethylation product **25** is formed along with the bromide **24** (67% yield) when using the $Br_2/Ag_2SO_4/H_2SO_4$ system as the brominating agent. 4-Chloroquinoline (**19a**) in both cases gives a mixture of brominated compounds difficult to separate into individual components. According to ^{1}H NMR spectroscopy, the 7-bromide is the predominant product. Indeed, upon treating this mixture with dimethylamine, we isolated 7-bromo-4-dimethylaminoquinoline (**26**) as a pure compound.



Since the bromination of 4-R-quinolines does not affect position 5, we turned our attention to the nitration of 4-chloroquinolines **19a-c**. The literature data on this question are contradictory. There have been reports that the nitration of 4-chloroquinoline **19a** by the nitrating mixture of concentrated nitric and sulfuric acids at -5° to 0°C gives a mixture of 8-nitro- (**27a**) and 5-nitro-4-chloroquinolines (**28a**) in 59 and 20% yield, respectively [35-37].



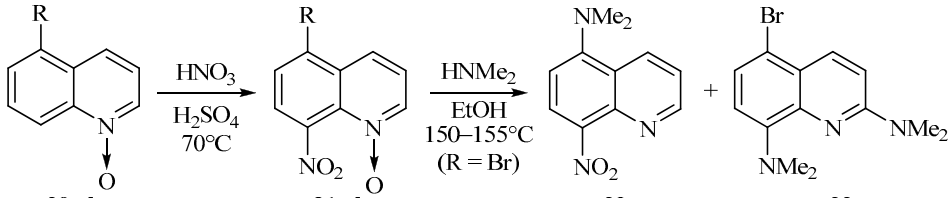
19, **27**–**29** **a** R = H; **b** R = Cl; **c** R = Me

On the other hand, Simpson and Wright [38] reported that only the 8-nitro isomer was obtained at -15°C in 28% yield. We found that chloride **19a** reacts with the nitrating mixture at 20°C to give exclusively 8-nitro derivative **27a**, while lowering the reaction temperature to 0°C leads to a 95:5 mixture of chloroquinolines **27a** and **28a**. While 8-nitro derivative **27a** could be readily isolated as a pure compound by fractional recrystallization from ethanol, 5-nitro derivative **28a** could not be isolated as a pure compound even by chromatography.

The nitration of 2,4-dichloroquinoline (**19b**) requires more vigorous conditions than the analogous reaction of 4-chloroquinoline (**19a**). The reaction for 2,4-dichloroquinoline begins only upon heating the reaction mixture to 60°C and leads to a 73:11:16 mixture of 8-nitro- (**27b**), 5-nitro- (**28b**), and 7-nitro-2,4-dichloroquinolines (**29b**) with 68% overall yield. Isomers **27b** and **29b** were isolated as pure compounds by fractional crystallization from isooctane and ethanol, while the desired product, namely, 2,4-dichloro-5-nitroquinoline (**28b**) could not be separated from other isomers.

The nitration of 4-chloro-2-methylquinoline (**19c**) has been described by Adams [39] and Denny [40]. These authors reported the formation of two isomers, specifically, 5-nitro- (**28c**) and 8-nitro-4-chloro-2-methylquinolines (**27c**). Our results show that the nitration of chloroquinoline **19c** by the nitrating mixture at 20°C leads exclusively to 8-nitro derivative **27c** in almost quantitative yield. The same reaction at 0°C gives an 87:6:7 mixture of compounds **27c, 28c,** and **29c** with 80% overall yield. Column chromatography on silica gel using chloroform as the eluent gave 4-chloro-2-methyl-8-nitroquinoline **27c** as a pure compound, while isomers **28c** and **29c** could not be separated.

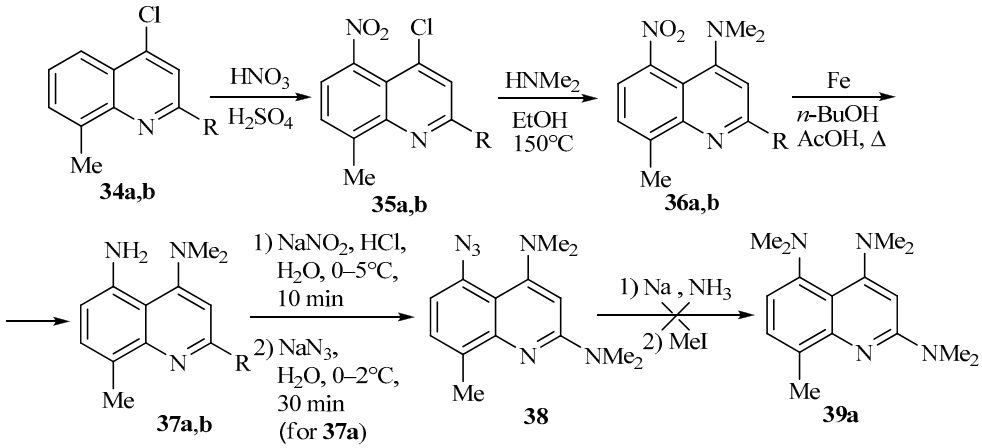
Use of 5-haloquinoline *N*-oxides. Quinoline 1-oxide is known to be nitrated at position 4 at 60°C [27]. We anticipated that the nitration of 5-haloquinoline *N*-oxides **30a**,**b** would proceed similarly. However, this reaction unfortunately led to 5-halo-8-nitroquinoline 1-oxides **31a**,**b** as the only products as indicated by ^{1}H NMR spectroscopy and the chemical properties of these oxides. In particular, heating oxide **31b** with excess of dimethylamine in ethanol in a sealed ampoule at 150-155°C gave a mixture of 5-dimethylamino-8-nitroquinoline (**32**) and 5-bromo-2,8-bis(dimethylamino)quinoline (**33**), indicating that the bromine and hydrogen atoms as well as the nitro group may undergo nucleophilic aromatic substitution in this compound.



30, 31 a R = Cl; **b** R = Br

Synthesis of 4,5-bis(dimethylamino)-8-methyl-2-R-quinolines. Hence, the synthesis of 4,5-bis-(dimethylamino)quinolines may be simplified when a substituent is present at position 8. In this case, the nitration of suitable precursors should proceed exclusively at position 5. This assumption proved entirely correct for diamines **37a**,**b**, which we synthesized by the consecutive nitration of 4-chloro-8-methylquinolines **34a**,**b**, following substitution of chlorine by a dimethylamino group in the resultant 5-nitroquinolines **35a**,**b**, and reduction of the obtained nitro compounds **36a**,**b** [41].

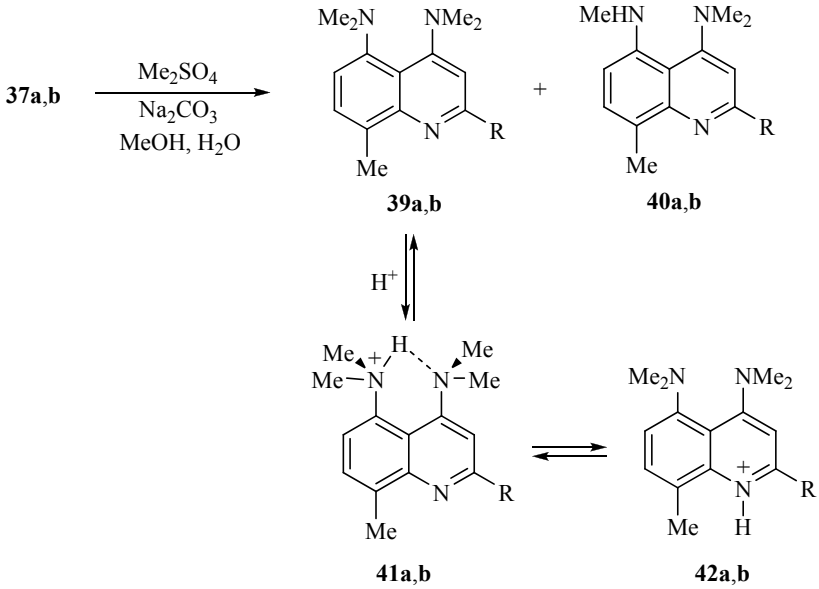
We were unable to carry out the methylation of amine **37a** using two equivalents of iodomethane in liquid ammonia in the presence of sodium amide, which is probably a consequence of the low acidity of the 5-NH_2 group. Only the starting compound could be isolated from the reaction mixture. Another alkylation method proposed for primary aryl- and hetarylamines with low NH acidity entails prior conversion of the amine to an azide, reduction of this azide by sodium in liquid ammonia to give the dianion, and treatment of this intermediate with an alkyl halide [42]. We obtained azide **38** in good yield but, unfortunately, only tar formation ensued upon the action of sodium in liquid ammonia on this compound.



34, **35** **a** R = Cl, **b** R = Me; **36**, **37** **a** R = NMe_2, **b** R = Me

The target compounds **39a**,**b** were obtained by methylation of amines **37a**,**b** using excess dimethyl sulfate in methanol in the presence of sodium carbonate. This reaction proceeds rather slowly and monomethylation products **40a** (9% yield) and **40b** (21% yield) were also isolated and characterized. Our recent brief communication concerning the synthesis of compounds **39a**,**b** was recently published.

Quinolines **39a**,**b** readily form picrates and perchlorates. An X-ray structural analysis of the picrates (CCDC deposits 888288 and 888289 at the Cambridge Crystallographic Data Center) showed that the picrate of base **39a** has structure **41a**, where the proton is chelated by two *peri*-NMe_2 groups as in ordinary proton sponges. On the other hand, diamine **39b** forms picrate **42b**·**PicO**$^-$, in which the proton is localized next to nitrogen atom of the heterocycle.



37, **39**, **41**, **42** **a** R=NMe_2, **b** R=Me

More complicated behavior is observed upon the protonation of *peri*-diamines **39a**,**b** in solution. The ^{1}H NMR spectra of the picrate and perchlorate of compound **39a** show an equilibrium of two protonated forms (**41a** ⇄ **42a**). The ratio of these forms depends on the polarity of the solvent (Table 2). In low-polarity solvents, like $CDCl_3$ and $ClCD_2CD_2Cl$, cation **42a** predominates, while in more polar solvents, like CD_3CN, DMSO-d_6, and CD_3COCD_3, the contents of both forms becomes comparable. Under the same conditions, the salts of

4,5-bis(dimethylamino)-2,8-dimethylquinoline (**39b**) are protonated only at the nitrogen atom in heterocycle (form **42b**). Switching from apolar to polar solvents does not lead to the appearance of any substantial concentration of form **41b**.

TABLE 2. Chemical Shifts of the NH Protons in the ^{1}H NMR Spectra of the Picrate of Diamine **39a** and the Contents of Protonated Forms **41a** and **42a**

Solvent	The dipole moment of the solvent, D	δ_{NH}, ppm		The content of the protonated forms, %	
		41a	**42a**	**41a**	**42a**
$CDCl_3$	1.15	17.07	9.12	15	85
$ClCD_2CD_2Cl$	1.85	17.45	8.01	5	95
CD_3CN	3.38	17.37	8.17	50	50
DMSO-d_6	4.26	17.07	9.12	55	45
DMSO-d_6*	4.26	17.07	9.12	55	45
Acetone-d_6	2.70	17.78	8.85	58	42

An unexpected result was discovering much higher basicity of diamine **39b** in comparison to **39a**. The ionization constants pK_a were determined by the competitive method [43, 44]. The pK_a value for diamine **39b** for protonation at the nitrogen atom in the ring was found to be 7.2, which is only slightly less than the basicity of naphthalene proton sponge **1**. The pK_a values of diamine **39a** corresponding to protonation of the *peri*-dimethylamino groups and ring nitrogen atom are equal to 6.5 and 6.3, respectively. We assume that solvation of the NH proton in form **42a** is markedly hindered in the salt derivatives of compound **39a** due to the steric effect of the branched 2-NMe_2 group together with the 8-Me group. It is precisely this effect, which leads to relative destabilization of this form and produces conditions for protonation of the molecule at the *peri*-NMe_2 groups. This behavior is entirely analogous to the drop in basicity when going from 2,6-dimethylpyridine to 2,6-diisopropylpyridine and 2,6-di-*tert*-butylpyridine [45]. This explanation can also account for the particularly remarkable finding; low rate of interconversion of forms **41** and **42** on the NMR time scale when the NH protons corresponding to these forms appear as separate though slightly broadened peaks. The activation energy for proton transfer in this case is close to 20 kcal/mol [46]. It is known that the protonation-deprotonation of ordinary amines [47] and even sterically unhindered *peri*-diaminonaphthalenes [48] proceeds at a rate close to diffusion.

Thus, we have synthesized the first two representatives of 4,5-bis(dimethylamino)quinolines and shown that the direction of their protonation significantly depends on the aggregate state, solvent used, and nature of the substituents on the quinoline ring. We are the first to report the protonation of dimethylamino groups conjugated with the heteroatom in the azine series for the case of 2,4,5-tris(dimethylamino)-8-methylquinoline, i.e., this diamine displays proton sponge properties.

EXPERIMENTAL

The IR spectra were recorded on an FSM-1202 spectrometer for vaseline mulls. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-250 spectrometer (250 and 62.9 MHz, respectively) in DMSO-d_6 (perchlorates and picrates of compounds **39a**,**b**) and $CDCl_3$ (other compounds) with TMS as internal standard. The electron impact mass spectra were recorded on a Finnigan MAT INCOS 50 mass spectrometer at 70 eV. The combustion elemental analysis was carried out by the Pregl–Dumas method. The melting points were determined in glass capillaries on an SMP 30 apparatus. The purity of the products and the course of the

reactions were followed by thin-layer chromatography on Brockmann grade IV alumina plates using chloroform as the eluent. Acroseal™ *n*-butyllithium in hexane supplied by Acros, a solution of *t*-butyllithium in pentane supplied by Sigma-Aldrich, and 99% 5-aminoquinoline supplied by Alfa Aesar were used in this work.

4-Dimethylaminoquinoline (6). Liquid dimethylamine (1.1 ml) was added to a solution of 4-chloroquinoline (0.344 g, 2.1 mmol) in ethanol (3 ml) at -10°C. The mixture was transferred to a glass ampoule, sealed, and maintained at 150-155°C for 3 h. Upon cooling, the ampoule was opened. The mixture was evaporated to dryness, and the residue was dissolved in a minimal amount of methylene chloride. The solution was passed through an alumina column using CH_2Cl_2 as the eluent. The first fraction eluted contained 0.045 g (13%) starting 4-chloroquinoline, R_f 0.9. The second fraction gave 0.21 g (58%) 4-dimethylaminoquinoline (**6**) as a viscous yellow oil, R_f 0.4. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.94 (6H, s, NMe_2); 6.73 (1H, d, J = 5.3, H-3); 7.40-7.46 (1H, m, H-7); 7.58-7.64 (1H, m, H-6), 8.03 (2H, m, H-5,8); 8.64 (1H, d, J = 4.6, H-2). The other spectral characteristics of this compound correspond to the values reported by McCurdy et al. [13].

Reaction of 4-Dimethylaminoquinoline (6) with *n*-BuLi and *t*-BuLi (General Method). 1.6 M *n*-butyllithium (0.31 ml, 0.5 mmol) in hexane or 1.7 M *t*-butyllithium (0.29 ml, 0.5 mmol) in pentane was added to a solution of 4-dimethylaminoquinoline (**6**) (0.034 g, 0.2 mmol) in absolute ether (2 ml) under an argon atmosphere at -15°C. At the end of the reaction, water (0.5 ml) was added, and the mixture was maintained for 1 h at 20°C. The ethereal layer was removed, and the solvent was distilled off. The residue was subjected to chromatography on alumina using CH_2Cl_2 as the eluent.

2-*n*-Butyl-2,3-dihydroquinolin-4-one (8a) was obtained according to the general procedure from amine **6** and *n*-butyllithium. The reaction mixture was maintained for 1 h at -15°C. Yield 0.034 g (85%), pale-yellow crystals, mp 65-67°C (octane). IR spectrum, ν, cm^{-1}: 1658 (C=O), 3335 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91 (3H, t, J = 6.9, $(CH_2)_3C\underline{H}_3$); 1.28-1.37 (4H, m, $(C\underline{H}_2)_2CH_3$); 1.59-1.67 (2H, m, $C\underline{H}_2(CH)_2CH_3$); 2.45 (1H, dd, ^2J = 16.1, ^3J = 12.6) and 2.65 (1H, dd, ^2J = 16.1, ^3J = 3.8, 3-CH_2); 3.54-3.66 (1H, m, 2-CH); 4.32 (1H, br. s, NH); 6.64 (1H, d, J = 8.5, H-8); 6.67-6.73 (1H, m, H-6); 7.24-7.30 (1H, m, H-7); 7.79 (1H, d, J = 7.6, H-5). Mass spectrum, *m*/*z* (I_{rel}, %): 203 $[M]^+$ (25), 146 $[M\text{-}Bu]^+$ (100). Found, %: C 76.83; H 8.45; N 6.90. $C_{13}H_{17}NO$. Calculated, %: C 76.81; H 8.43; N 6.89.

2-*t*-Butyl-2,3-dihydroquinolin-4-one (8b) was obtained according to the general procedure from amine **6** and *t*-butyllithium. The reaction mixture was maintained for 1 h at -15°C. Yield 0.024 g (60%), pale-yellow crystals, mp 148-149°C (octane). IR spectrum, ν, cm^{-1}: 1659 (C=O), 3352 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 (9H, s, $C(CH_3)_3$); 2.49 (1H, dd, ^2J = 15.9, ^3J = 13.8) and 2.63 (1H, dd, ^2J = 15.9, ^3J = 3.7, 3-CH_2); 3.27-3.35 (1H, m, 2-CH); 4.31 (1H, br. s, NH); 6.66-6.74 (2H, m, H-6,8); 7.24-7.32 (1H, m, H-7); 7.79 (1H, dd, ^3J = 7.9, ^4J = 1.7, H-5). Mass spectrum, *m*/*z* (I_{rel}, %): 203 $[M]^+$ (8), 146 $[M\text{-}Bu]^+$ (100). Found, %: C 76.82; H 8.44; N 6.91. $C_{13}H_{17}NO$. Calculated, %: C 76.81; H 8.43; N 6.89.

2-*n*-Butyl-4-dimethylaminoquinoline (9) was obtained according to the general procedure from amine **6** and *n*-butyllithium. The reaction mixture was maintained for 96 h at 20°C. Yield 0.029 g (63%), yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.94 (3H, t, J = 7.4, $(CH_2)_3C\underline{H}_3$); 1.35-1.50 (2H, m, $(CH_2)_2C\underline{H}_2CH_3$); 1.69-1.82 (2H, m, $CH_2C\underline{H}_2CH_2CH_3$); 2.86 (2H, t, J = 8.1, $C\underline{H}_2(CH)_2CH_3$); 2.99 (6H, s, $N(CH_3)_2$); 6.65 (1H, s, H-3); 7.33-7.40 (1H, m, H-7); 7.54-7.60 (1H, m, H-6); 7.94-8.00 (2H, m, H-5,8). Mass spectrum, *m*/*z* (I_{rel}, %): 228 $[M]^+$ (8), 186 $[M\text{-}C_3H_6]^+$ (100). Found, %: C 78.89; H 8.83; N 12.28. $C_{15}H_{20}N_2$. Calculated, %: C 78.90; H 8.83; N 12.27.

5-Dimethylaminoquinoline (11). Finely cut sodium (0.107 g, 4.7 mmol) and several crystals of ferric nitrate were added to liquid ammonia (10 ml). As soon as the mixture became colorless, 5-aminoquinoline (**10**) (0.288 g, 2 mmol) was added. After 5 min, iodomethane (0.26 ml, 0.528 g, 4 mmol) was added. The mixture was stirred for 1 h. Cooling was then discontinued, permitting ammonia to evaporate freely. The residue was subjected to chromatography on an alumina column using CH_2Cl_2 as the eluent and collecting two fractions. The first fraction (R_f 0.7) contained dimethylaminoquinoline **11**. Yield 0.261 g (76%), yellow-brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.87 (6H, s, $N(CH_3)_2$); 6.48 (1H, dd, ^3J = 8.3, ^4J = 0.9, H-6); 7.34-7.39 (1H, m, H-3); 7.56-7.62 (1H, m, H-7); 7.74 (1H, d, J = 8.5, H-8); 8.52 (1H, dd, ^3J = 8.5, ^4J = 1.6, H-4); 8.85 (1H, dd,

^3J = 8.5, ^4J = 1.6, H-2). Found, %: C 76.69; H 7.05; N 16.26. $C_{11}H_{12}N_2$. Calculated, %: C 76.71; H 7.02; N 16.27. The second fraction (R_f 0.4) contained the starting 5-aminoquinoline **10**. Yield 0.057 g (20%), as gray-brown crystals.

2-*n*-Butyl-1,2-dihydro-5-dimethylaminoquinoline (13a) and 2-*n*-butyl-5-dimethylaminoquinoline (14a) were obtained from amine **11** and *n*-butyllithium according to the general method given above for the metallation of amine **6**. The mixture was maintained for 96 h at 20°C. After evaporation of ether, the residue was dissolved in CH_2Cl_2 and subjected to chromatography on an alumina column using 1:1 CH_2Cl_2–hexane as the eluent. The first fraction (R_f 0.9) gave 1,2-dihydroquinoline **13a**. Yield 0.035 g (76%), dark-yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.89 (3H, t, *J* = 7.4, $(CH_2)_3C\underline{H}_3$); 1.31-1.36 (4H, m, $(C\underline{H}_2)_2CH_3$); 1.53-1.59 (2H, m, $C\underline{H}_2(CH_2)_2CH_3$); 2.69 (6H, s, $N(CH_3)_2$); 4.03-4.10 (1H, m, 2-CH); 5.54-5.59 (1H, m, 3-CH); 6.14 (1H, d, *J* = 7.9, 4-CH); 6.28 (1H, dd, ^3J = 8.1, ^4J = 0.9, H-6); 6.64 (1H, dd, ^3J = 9.9, ^4J = 0.8, H-8); 6.85-6.92 (1H, m, H-7). Found, %: C 78.20; H 9.61; N 12.17. $C_{15}H_{22}N_2$. Calculated, %: C 78.21; H 9.63; N 12.16. The second fraction (R_f 0.7) gave quinoline **14b**. Yield 0.008 g (18%), yellow-brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.95 (3H, t, *J* = 7.4, $(CH_2)_3C\underline{H}_3$); 1.39-1.48 (2H, m, $(CH_2)_2C\underline{H}_2CH_3$); 1.72-1.84 (2H, m, $CH_2C\underline{H}_2CH_2CH_3$); 2.95 (2H, t, *J* = 8.1, $C\underline{H}_2(CH_2)_2CH_3$); 2.86 (6H, s, $N(C\underline{H}_3)_2$); 7.02 (1H, dd, ^3J = 7.5, ^4J = 1.1, H-6); 7.26 (1H, d, *J* = 8.8, H-3); 7.52-7.58 (1H, m, H-7); 7.67-7.71 (1H, m, H-8); 8.42 (1H, dd, ^3J = 9.1, ^4J = 0.7, H-4). Mass spectrum, *m*/*z* (I_{rel}, %): 228 $[M]^+$ (21), 186 $[M\text{-}C_3H_6]^+$ (100). Found, %: C 78.89; H 8.84; N 12.25. $C_{15}H_{20}N_2$. Calculated, %: C 78.90; H 8.83; N 12.27.

2-*tert*-Butyl-1,2-dihydro-5-dimethylaminoquinoline (13b) and 2-*tert*-butyl-5-dimethylaminoquinoline (14b) were obtained analogously from amine **11** and *tert*-butyllithium. The residue after evaporation of ether was dissolved in CH_2Cl_2 and subjected to chromatography on an alumina column using 2:1 CH_2Cl_2–hexane as the eluent. The first fraction (R_f 0.9) gave 1,2-dihydroquinoline **13b**. Yield 0.035 g (76%), dark-yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (9H, s, $C(C\underline{H}_3)_3$); 2.68 (6H, s, $N(CH_3)_2$); 3.83 (1H, d, *J* = 4.4, 2-CH); 3.98 (1H, br. s, NH); 5.56 (1H, dd, ^3J = 10.2, ^3J = 4.6, 3-CH); 6.08-6.12 (1H, m, H-8); 6.22 (1H, dd, ^3J = 8.1, ^4J = 0.9, H-6); 6.73 (1H, ddd, ^3J = 10.2, ^4J = 1.3, ^5J = 0.7, 4-CH); 6.82-6.89 (1H, m, H-7). Found, %: C 78.20; H 9.62; N 12.16. $C_{15}H_{22}N_2$. Calculated, %: C 78.21; H 9.63; N 12.16. The second fraction (R_f 0.7) gave quinoline **14b**. Yield 0.008 g (17%), yellow-brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.45 (9H, s, $C(CH_3)_3$); 2.86 (6H, s, $N(CH_3)_2$); 7.01 (1H, dd, ^3J = 7.5, ^4J = 0.8, H-6); 7.48 (1H, d, ^3J = 8.9, H-3); 7.50-7.56 (1H, m, H-7); 7.71 (1H, d, *J* = 8.4, H-8); 8.42 (1H, d, *J* = 8.9, H-4). Found, %: C 78.88; H 8.82; N 12.24. $C_{15}H_{20}N_2$. Calculated, %: C 78.90; H 8.83; N 12.27.

Metallation of 4-dimethylaminoquinoline (6) at -78°C was carried out according to the general method using *n*-butyllithium (reaction time 2 h) or *tert*-butyllithium (reaction time 1 h). At the end of the reaction, CD_3OD (0.5 ml) was added, and the mixture was maintained for 20 min at -78°C and then, cooling was discontinued. After warming to room temperature, D_2O (0.5 ml) was added. After 1 h, the ethereal layer was separated, and ether was evaporated off. The ^{1}H NMR spectrum of the product was identical to the spectrum of dimethylaminoquinoline **6** with the exception of reduced integral intensity of the signal H-2 at 8.64 ppm by 18% (from *n*-butyllithium) and by 21% (from *tert*-butyllithium), which indicates the presence of ~18-21% of 2-deutero-4-dimethylaminoquinoline (**15a**) in the reaction mixture.

Metallation of 5-dimethylaminoaminoquinoline (11) at -78°C was carried out as described above for 4-dimethylaminoquinoline (**6**). The ^{1}H NMR spectrum of the product was identical to the spectrum of dimethylaminoquinoline **11** with the exception of a decrease in the integral intensity of the signal H-8 at 7.74 ppm by 22% (from *n*-butyllithium) and by 17% (from *tert*-butyllithium) and the signal for H-2 at 8.85 ppm by 15% (from *n*-butyllithium) and by 20% (from *tert*-butyllithium). This result indicates the presence of ~17-22% of 8-deutero-5-dimethylaminoquinoline (**16**) and ~15-20% of 2-deutero-5-dimethylaminoquinoline (**15b**) in the reaction mixture.

4-Chloroquinoline (19a) and 2,4-Dichloroquinoline (19b). PCl_3 (4.5 ml) was added to a solution of 4-nitroquinoline 1-oxide **18** [17] (3.1 g, 16.3 mmol) in chloroform (35 ml) cooled to 0°C. The mixture was heated at reflux for 1 h. Upon cooling, the mixture was neutralized by adding 5% aqueous sodium hydroxide

(20 ml). The chloroform layer was separated, and the solvent was distilled off. The residue was subjected to chromatography on an alumina column using 1:2 CH_2Cl_2–hexane as the eluent. The first fraction (R_f 0.8) gave dichloroquinoline **19b**. Yield 1.014 g (31%), colorless crystals, mp 63-64°C (petroleum ether) (mp 67°C [49]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.49 (1H, s, H-3); 7.60-7.66 (1H, m, H-7); 7.74-7.81 (1H, m, H-6); 8.02 (1H, dd, ^3J = 8.4, ^4J = 1.4, H-5); 8.18 (1H, dd, ^3J = 8.8, ^4J = 1.4, H-8). The second fraction (R_f 0.5) gave 4-chloroquinoline **19a**. Yield 1.754 g (66%), pale-yellow oil, which crystallized upon cooling. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.46 (1H, d, *J* = 4.6, H-3); 7.58-7.65 (1H, m, H-7); 7.71-7.78 (1H, m, H-6); 8.05 (1H, d, *J* = 8.1, H-5); 8.21 (1H, dd, ^3J = 8.4, ^4J = 1.4, H-8); 8.76 (1H, d, *J* = 4.6, H-2). The spectral characteristics of 4-chloroquinoline (**19a**) corresponded to the data given by Ruchelman et al. [37].

4,5-Dinitroquinoline 1-oxide (22). A mixture of 86% nitric acid (0.61 ml, 13.3 mmol) and concentrated sulfuric acid (1.47 ml, 27 mmol) was added to a solution of 5-nitroquinoline 1-oxide (**21**) [50] (2.114 g, 11.1 mmol) in concentrated sulfuric acid (15 ml). The mixture was stirred for 16 h at 130-140°C and then poured onto ice (50 g). The precipitate was filtered off and washed thoroughly with water. The resultant mixture of oxides **21** and **22** was separated by preparative thin-layer chromatography on alumina using chloroform as the eluent. The first fraction with R_f 0.7 gave 4,5-dinitroquinoline 1-oxide (**22**) (0.240 g, 10%) and the second fraction with R_f 0.5 gave starting *N*-oxide **21**. Oxide **22** was obtained as pale-yellow crystals, mp 232-235°C (*n*-BuOH) (260-262°C (AcOH) [27]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.95 (1H, dd, ^3J = 8.8, ^3J = 7.7, H-7); 8.08 (1H, d, *J* = 6.9, H-3); 8.39 (1H, dd, ^3J = 7.7, ^4J = 1.3, H-6); 8.55 (1H, d, *J* = 6.9, H-2); 9.01 (1H, dd, ^3J = 8.8, ^4J = 1.1, H-8). Found, %: C 45.95; H 2.18; N 17.77. $C_9H_5N_3O_5$. Calculated, %: C 45.97; H 2.14; N 17.87.

General Method for the Bromination of 4-R-Quinolines. NBS (0.196 g (1.1 mmol) (method A) or Ag_2SO_4 (0.312 g, 1 mmol) and Br_2 (0.057 ml, 1 mmol) (method B) was added to a solution of 4-R-quinoline (1 mmol) in concentrated sulfuric acid (2 ml). The mixture was maintained at 20°C for 48 h (method A) or 24 h (method B) and then poured onto ice (10 g). The mixture was neutralized by adding concentrated ammonium hydroxide and extracted with chloroform. The product was purified as described below.

3-Bromo-4-dimethylaminoquinoline (24) was obtained as a yellow oil according to method A from amine **6**. The product was purified by chromatography on an alumina column using 2:1 CH_2Cl_2–hexane as the eluent, R_f 0.9. Yield 0.2 g (80%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.11 (6H, s, NMe_2); 7.46-7.52 (1H, m, H-7); 7.60-7.67 (1H, m, H-6); 8.01 (1H, d, *J* = 8.5, H-5); 8.09 (1H, d, *J* = 8.5, H-8); 8.77 (1H, s, H-2). Mass spectrum, *m*/*z* (I_{rel}, %): 252 [M (^{81}Br)]$^+$ (88), 250 [M (^{79}Br)]$^+$ (100), 171 [M-Br]$^+$ (96). Found, %: C 52.62; H 4.41; Br 31.81; N 11.17. $C_{11}H_{11}BrN_2$. Calculated, %: C 52.61; H 4.42; Br 31.82; N 11.16.

3-Bromo-4-methylaminoquinoline (25) was obtained as the minor product (0.012 g, 5%) in a mixture with the major product, dimethylaminoquinoline **24** (obtained in 67% yield) upon the bromination of amine **6** according to method B. Methylaminoquinoline **25** was purified to remove dimethylaminoquinoline **24** by chromatography on an alumina column using 2:1 CH_2Cl_2–hexane as the eluent. The fraction with R_f 0.7 gave methylaminoquinoline **25**. Yellow-orange crystals, mp 127-128°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.38 (3H, d, *J* = 5.7, CH_3); 4.99 (1H, br. s, NH); 7.39-7.45 (1H, m, H-7); 7.58-7.65 (1H, m, H-6); 7.96 (1H, d, *J* = 8.4, H-5); 8.14 (1H, d, *J* = 8.5, H-8); 8.64 (1H, s, H-2). Mass spectrum, *m*/*z* (I_{rel}, %): 238 [M (^{81}Br)]$^+$ (92), 236 [M (^{79}Br)]$^+$ (100), 156 [M-Br]$^+$ (63). Found, %: C 50.65; H 3.81; Br 33.72; N 11.83. $C_{10}H_9BrN_2$. Calculated, %: C 50.66; H 3.83; Br 33.70; N 11.82.

7-Bromo-4-dimethylaminoquinoline (26) was obtained during treatment of the crude mixture obtained upon the bromination of 4-chloroquinoline (**19a**) according to method A or B with subsequent evaporation of chloroform to dryness, with dimethylamine (3 ml) and ethanol (2 ml). The mixture was transferred to a sealed ampoule, heated at 150-155°C for 6 h, and then evaporated. The residue was subjected to chromatography using CH_2Cl_2 as the eluent. The fraction with R_f 0.9 gave dimethylaminoquinoline **26**. Yield 0.198 g (79%), yellow-orange oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.98 (6H, s, CH_3); 6.73 (1H, d, *J* = 5.2, H-3); 7.65 (1H, dd, ^3J = 9.0, ^4J = 2.2, H-6); 7.86 (1H, d, *J* = 9.0, H-5); 8.17 (1H, d, *J* = 2.2, H-8); 8.61 (1H, d, *J* = 5.2, H-2). Mass

spectrum, *m*/*z* (I_{rel}, %): 252 [M (^{81}Br)]$^+$ (81), 250 [M (^{79}Br)]$^+$ (83), 171 [M-Br]$^+$ (100). Found, %: C 52.60; H 4.41; Br 31.82; N 11.18. $C_{11}H_{11}BrN_2$. Calculated, %: C 52.61; H 4.42; Br 31.82; N 11.16.

2,4-Dichloro-8-nitroquinoline (27b) and 2,4-Dichloro-7-nitroquinoline (29b). A mixture of fuming nitric acid (0.11 ml, 2.8 mmol) and concentrated sulfuric acid (0.24 ml, 4.4 mmol) was added dropwise to a solution of 2,4-dichloroquinoline (**19b**) (0.396 g, 2 mmol) in concentrated sulfuric acid (3 ml) at 50°C. The temperature was raised to 60°C. The mixture was stirred for 8 h and poured onto a mixture of ice (100 g) and ammonium hydroxide (12 ml). The yellow-green precipitate consisting of a mixture of 5-, 7-, and 8-nitro-2,4-dichloroquinolines was filtered off. Consecutive recrystallization from isooctane and ethanol gave pure 2,4-dichloro-7-nitroquinoline (**29b**). Yield 0.053 g (11%), colorless crystals, mp 188-190°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.66 (1H, s, H-3); 8.16 (1H, d, J = 9.2, H-5); 8.54 (1H, dd, ^3J = 9.2, ^4J = 2.5, H-6); 9.12 (1H, d, J = 2,2, H-8). Found, %: C 44.50; H 1.69; Cl 29.15; N 11.51. $C_9H_4Cl_2N_2O_2$. Calculated, %: C 44.48; H 1.66; Cl 29.17; N 11.53.

The residue after evaporation of the ethanol was recrystallized from isooctane to give 2,4-dichloro-8-nitroquinoline (**27b**). Yield 0.238 g (49%), fine colorless needles, mp 103-105°C (isooctane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.64 (1H, s, H-3); 7.72 (1H, dd, ^3J = 8.5, ^3J = 7.6, H-6); 8.09 (1H, dd, ^3J = 7.6, ^4J = 1.4, H-5); 8.41 (1H, dd, ^3J = 8.5, ^4J = 1.3, H-7). Found, %: C 44.51; H 1.68; Cl 29.19; N 11.51. $C_9H_4Cl_2N_2O_2$. Calculated, %: C 44.48; H 1.66; Cl 29.17; N 11.53.

4-Chloro-2-methyl-8-nitroquinoline (27c) was obtained analogously to dichloroquinoline **27b** from 4-chloro-2-methylquinoline **19c** (0.355 g, 2 mmol) at 20°C for 1.5 h. Yield 0.432 g (97%), pale-yellow crystals, mp 111-113°C (mp 112-113°C [40]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.72 (3H, s, CH_3); 7.50 (1H, s, H-3); 7.61 (1H, dd, ^3J = 8.4, ^3J = 7.6, H-6); 7.96 (1H, dd, ^3J = 7.5, ^4J = 1.3, H-5); 8.37 (1H, dd, ^3J = 8.5, ^4J = 1.3, H-7).

5-Haloquinoline 1-oxides were obtained from 5-haloquinolines [51] analogously to the procedure for obtaining 5-bromoquinoline 1-oxide (**30b**) [52].

5-Chloroquinoline 1-oxide (30a). Pale-yellow crystals, mp 135-137°C (isooctane). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.35 (1H, dd, J = 8.7, J = 6.1, H-3); 7.73-7.55 (2H, m, H-6,7); 8.07 (1H, d, J = 8.7, H-4); 8.52 (1H, d, J = 6.0, H-2); 8.65 (1H, d, J = 8.4, H-8).

5-Chloro-8-nitroquinoline 1-oxide (31a) was obtained analogously to oxide **22** from 5-chloroquinoline 1-oxide **30a** (0.359 g, 2 mmol) at 70-80°C for 3 h. Yield 0.426 g (95%), yellow-green crystals, mp 229-232°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.53 (1H, dd, ^3J = 8.8, ^3J = 6.0, H-3); 7.65 (1H, d, J = 8.1, H-6); 7.76 (1H, d, J = 8.2, H-7); 8.16 (1H, d, J = 8.8, H-4); 8.52 (1H, d, J = 6.0, H-2). Found, %: C 48.15; H 2.27; Cl 15.80; N 12.49. $C_9H_5ClN_2O_3$. Calculated, %: C 48.13; H 2.24; Cl 15.78; N 12.47.

5-Bromo-8-nitroquinoline 1-oxide (31b) was obtained from *N*-oxide **30b** (0.224 g, 1 mmol) analogously to *N*-oxides **22** and **31a** at 55-60°C for 3 h. Yield 0.148 g (55%), yellow crystals, mp 228-229°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.50-7.56 (1H, m, H-3); 7.58 (1H, d, J = 8.0, H-6); 7.96 (1H, d, J = 8.0, H-7); 8.14 (1H, d, J = 8.9, H-4); 8.50 (1H, d, J = 6.1, H-2). Mass spectrum, *m*/*z* (I_{rel}, %): 270 [M (^{81}Br)]$^+$ (86), 268 [M (^{79}Br)]$^+$ (100), 115 (92). Found, %: C 40.20; H 1.89; Br 29.73; N 10.44. $C_9H_5BrN_2O_3$. Calculated, %: C 40.18; H 1.87; Br 29.70; N 10.41.

5-Dimethylamino-8-nitroquinoline (32) and 5-Bromo-2,8-bis(dimethylamino)quinoline (33). A mixture of oxide **31b** (0.134 g, 0.5 mmol), ethanol (2 ml), and dimethylamine (2 ml) was placed into a sealed ampoule and heated at 150-155°C for 6 h. The solvent was evaporated off, and the residue was subjected to chromatography on an alumina column using CH_2Cl_2 as the eluent. The first fraction (R_f 0.9) gave quinoline **33** as a yellow-brown oil, which slowly crystallized upon storage in a refrigerator. Yield 0.046 g (34%), mp 73-74°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.06 (6H, s, 8-N(CH_3)$_2$); 3.23 (6H, s, 2-N(CH_3)$_2$); 6.82 (1H, d, J = 8.4, H-3); 6.90 (1H, d, J = 9.5, H-7); 7.31 (1H, d, J = 8.4, H-4); 8.19 (1H, d, J = 9.5, H-6). Mass spectrum, *m*/*z* (I_{rel}, %): 295 [M (^{81}Br)]$^+$ (48), 293 [M (^{79}Br)]$^+$ (50), 279 [M-Me]$^+$ (100). Found, %: C 53.10; H 5.47; Br 27.28; N 14.30. $C_{13}H_{16}BrN_3$. Calculated, %: C 53.07; H 5.48; Br 27.16; N 14.28.

The second fraction (R_f 0.6) gave nitroquinoline **32**. Yield 0.046 g (32%), yellow crystals, mp 56-57°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.00 (6H, s, N(CH_3)$_2$); 6.92 (1H, d, J = 8.5, H-6); 7.45 (1H, dd, ^3J = 8.6,

^3J = 4.2, H-3); 8.09 (1H, d, J = 8.5, H-7); 8.48 (1H, dd, ^3J = 8.5, ^4J = 1.6, H-4); 9.02 (1H, dd, ^3J = 4.1, ^4J = 1.3, H-2). Mass spectrum, *m*/*z* (I_{rel}, %): 217 $[M]^+$ (100), 187 $[M-2Me]^+$ (71). Found, %: C 60.79; H 5.11; N 19.32. $C_{11}H_{11}N_3O_2$. Calculated, %: C 60.82; H 5.10; N 19.34.

The syntheses for products **34**-**37**, **39**, **40a**,**b**, and the picrates and perchlorates of compounds **37a**,**b** were described in our previous work [41].

5-Azido-2,4-bis(dimethylamino)-8-methylquinoline (38). A solution of sodium nitrite (0.041 g, 0.6 mmol) in water (1 ml) was added to a solution of amine **37a** (0.127 g, 0.52 mmol) in concentrated hydrochloric acid (2 ml) cooled to 0-5°C. After 10 min, a solution of sodium azide (0.04 g, 0.61 mmol) in water (1 ml) was added. The mixture was maintained at 0-2°C for 30 min, neutralized by adding concentrated ammonium hydroxide, and extracted with hexane. The organic layer was subjected to chromatography on an alumina column using hexane as the eluent to give methylquinoline **38**. Yield 0.124 g (89%), pale-yellow oil. IR spectrum, ν, cm^{-1}: 2111 (N_3). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.55 (3H, s, 8-CH_3); 2.84 (6H, s, 4-N$(CH_3)_2$); 3.18 (6H, s, 2-N$(CH_3)_2$); 6.20 (1H, s, H-3); 6.81 (1H, d, J =7.6, H-6); 7.29 (1H, d, J = 7.6, H-7). Mass spectrum, *m*/*z* (I_{rel}, %): 270 $[M]^+$ (16), 227 $[M-N_3-H]^+$ (100). Found, %: C 62.23; H 6.73; N 31.11. $C_{14}H_{18}N_6$. Calculated, %: C 62.20; H 6.71; N 31.09.

Diamine 39a Perchlorate. Light-yellow crystals, mp 234-235°C (EtOH). ^{1}H NMR spectrum (indicates the presence of forms **41a** and **42a**), δ, ppm (*J*, Hz): 2.44 (3H, s, 8-Me, **42a**); 2.54 (3H, s, 8-Me, **41a**); 2.72 (6H, br. s, 5-NMe_2, **42a**); 2.98 (6H, d, J = 0.9, 4-NMe_2, **41a**); 3.02 (6H, s, 4-NMe_2, **42a**); 3.17 (6H, d, J = 3.6, 5-NMe_2, **41a**); 3.21 (6H, s, 2-NMe_2, **41a**); 3.28 (6H, s, 2-NMe_2, **42a**); 5.90 (1H, d, J = 1.9, H-3, **42a**); 6.81 (1H, d, J = 8.3, H-6, **42a**); 7.37 (1H, d, J = 8.2, H-7, **42a**); 7.45 (1H, s, H-3, **41a**); 7.55-7.62 (2H, m, H-6,7, **41a**); 9.12 (1H, br. s, NH, **42a**); 17.08 (1H, br. s, NH, **41a**).

Diamine 39a Picrate. Yellow-orange crystals, mp 198-200°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.44 (3H, s, 8-Me, **42a**); 2.54 (3H, s, 8-Me, **41a**); 2.72 (6H, br. s, 5-NMe_2, **42a**); 2.98 (6H, d, J = 0.9, 4-NMe_2, **41a**); 3.02 (6H, s, 4-NMe_2, **42a**); 3.17 (6H, d, J = 3.6, 5-NMe_2, **41a**); 3.21 (6H, s, 2-NMe_2, **41a**); 3.28 (6H, s, 2-NMe_2, **42a**); 5.90 (1H, d, J = 1.9, H-3, **42a**); 6.81 (1H, d, J = 8.3, H-6, **42a**); 7.37 (1H, d, J = 8.2, H-7, **42a**); 7.45 (1H, s, H-3, **41a**); 7.55-7.62 (2H, m, H-6,7, **41a**); 8.58 (2H, s, H PicO, **41a**, **42a**); 9.12 (1H, br. s, NH, **42a**); 17.08 (1H, br. s, NH, **41a**). Found, %: C 52.67; H 5.45; N 19.54. $C_{22}H_{27}N_7O_7$. Calculated, %: C 52.69; H 5.43; N 19.55.

D**iamine 39b Perchlorate**. Light-brown crystals, mp 157-158°C (EtOH). ^{1}H NMR spectrum (demonstrates the presence of only one form **42b**), δ, ppm (*J*, Hz): 2.46 (3H, s, 8-Me); 2.57 (3H, br. s, 5-NMe_2); 2.61 (3H, s, 2-Me); 2.91 (3H, br. s, 5-NMe_2); 2.99 (3H, br. s, 4-NMe_2); 3.28 (3H, br. s, 4-NMe_2); 6.87-6.90 (2H, m, H-3,7); 7.48 (1H, d, J = 8.2, H-6); 11.58 (1H, br. s, NH).

Diamine 39b Picrate (exists as the crystal monohydrate). Orange cubes, mp 95-97°C (EtOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.46 (3H, s, 8-Me); 2.57 (3H, br. s, 5-NMe_2); 2.61 (3H, s, 2-Me); 2.91 (3H, br. s, 5-NMe_2); 2.99 (3H, br. s, 4-NMe_2); 3.28 (3H, br. s, 4-NMe_2); 6.87-6.90 (2H, m, H-3,7); 7.48 (1H, d, J = 8.2, H-6); 8.58 (2H, s, H PicO); 11.58 (1H, br. s, NH). Found, %: C 51.42; H 5.33; N 17.15. $C_{21}H_{26}N_6O_8$. Calculated, %: C 51.43; H 5.34; N 17.13.

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