846 *Russian Chemical Bulletin, International Edition, Vol. 50, No. 5, pp. 846—853, May, 2001*

peri-Naphthylenediamines

31.* Study of interconversions of 2,3-dihydroperimidines and 1,8-bis(dialkylamino)naphthalenes. Convenient synthesis of 1,2,2,3-tetramethyl-2,3-dihydroperimidine and a monoisopropyl analog of the "proton sponge"

V. A. Ozeryanskii, E. A. Filatova, V. I. Sorokin, and A. F. Pozharskii*

Rostov State University,
7 ul. Zorge, 344090 Rostov-on-Don, Russian Federation.
Fax: +7 (863 2) 22 3958. E-mail: pozharsk@pozhar.rnd.runnet.ru

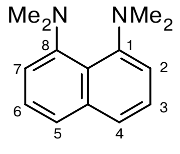
Efficient procedures were developed for the two-step synthesis of 1,2,2,3-tetramethyl-2,3-dihydroperimidines and for the one-step synthesis of 1,3-dimethyl-2,3-dihydroperimidines starting from 1,8-diaminonaphthalenes. New possibilities of the use of 2,3-dihydroperimidinium salts in the synthesis of 1,8-bis(dialkylamino)naphthalenes ("proton sponges") containing the *N*-isopropyl group along with the *N*-methyl groups were demonstrated. The 1,1,2,2,3-pentamethyl-2,3-dihydroperimidinium cation exists in the acyclic iminium form responsible for its high reactivity.

Key words: 1,8-diaminonaphthalenes, 2,3-dihydroperimidines, *N*-alkylation, *peri*-cyclization, 2,3-dihydroperimidinium salts, iminium cations, "proton sponges".

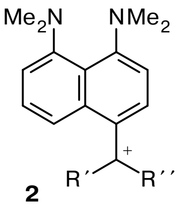
Previously, it has been demonstrated that 1,8-bis(dialkylamino)naphthalene (**1**), which is the so-called "proton sponge," possesses exceptionally high C-nucleophilicity in addition to abnormally high basicity.[2—4] The former property manifests itself not only in mild conditions under which electrophilic substitution proceeds (these reactions often take place at the temperature below −20 or even −40 °C and are accompanied by the formation of polysubstitution products), but also in the reactivity, which has been previously unknown for compounds of the naphthalene series. Cycloaddition of 4,5-bis(dimethylamino)-1-naphthylmethyl carbocations **2**[5] and the formation of naphtho[1,8-*c,d*]pyran derivatives in the reaction of diamine **1** with trifluoroacetic anhydride,[6] which we have discovered recently, are prominent examples.

The capability of two dimethylamino groups in compound **1** for efficiently donating electrons to the aromatic core is surprising the more so as not only NMe_2 groups but also the naphthalene ring, as such, are nonplanar. In this connection, it was of interest to study the C-nucleophilicity of electronic analogs of "proton sponge" **1** possessing minimum steric distortions. 1,2,2,3-Tetramethyl-2,3-dihydroperimidine (**3**)** is one of such structural analogs because the dihydroperimidine ring adopts a flattened boat conformation, which undergoes rapid inversion with a planar transition state.[8,9]

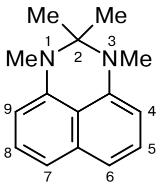
The aim of the present study was to develop a convenient procedure for the synthesis of compound **3** and its salt **4** as a model in which one benzene ring is activated, whereas another benzene ring is inactive with respect to electrophiles.



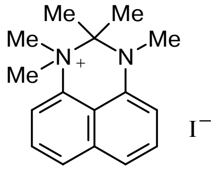
1



2



3



4

Results and Discussion

Two procedures for the preparation of compound **3** are available in the literature (Scheme 1). One proce-

---

[*] For Part 30, see Ref. 1.

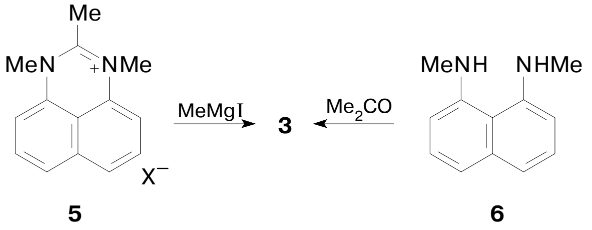
[**] 2,3-Dihydroperimidines, which do not contain substituents at position 2, cannot be used for this purpose because these compounds are readily dehydrogenated under the action of even mild electrophiles (see, for example, Ref. 7).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 5, pp. 809—816, May, 2001.

1066-5285/01/5005-846 $25.00

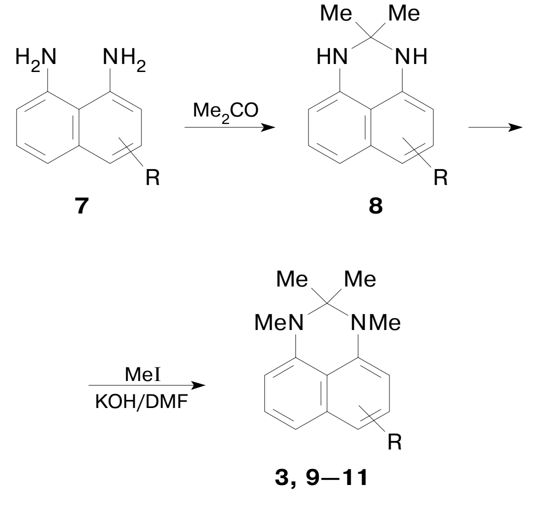
dure[10] consists in treatment of 1,2,3-trimethylperimidinium salts **5** with methylmagnesium iodide. Another procedure[11] involves condensation of 1,8-bis(methylamino)naphthalene (**6**) with acetone. However, in spite of good yields, both procedures have drawbacks among which are operations with organometallic compounds and the fact that the starting compounds **5** and **6** are rather difficultly accessible.

Scheme 1



In the present study, we developed a simple and efficient procedure for the synthesis of compound **3** and its derivatives **9—11** containing substituents in the aromatic core. This procedure is free of the above-mentioned drawbacks (Scheme 2).

Scheme 2

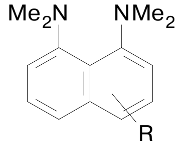


R = H (**3**), 5-NO_2(**9**), 6-NO_2(**10**), 6-NMe_2(**11**)

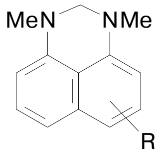
The synthesis involves 1,8-diaminonaphthalenes **7** as the starting substrates. These compounds readily react with acetone to form 2,2-dimethyl-2,3-dihydroperimidines **8**. Cyclization proceeds in quantitative yields upon simple mixing of the reagents or filtration of a solution of the corresponding diamine through a thin layer of Al_2O_3 using acetone as the eluent.[12] The reaction is virtually independent of the type and the number of substituents in the naphthalene ring and has been described previously for diamines **7** containing the H atom or the 2-chloro, 4-sulfo, 3,6-dinitro, or 2,4,5,7-tetranitro groups as substituents (see the review[13]). In the present study, we completed the series of substituents with the 3-nitro, 4-nitro, and 4-amino groups.

The subsequent reactions of dihydroperimidines **8** with MeI in DMF in the presence of KOH afforded the desired tetramethyl derivatives in 75—90% yields. The scheme is even more simplified because dihydroperimidines **8** can be obtained directly in the reaction flask and immediately introduced into the reaction with the alkylating agent without isolation. This one-pot process does not require expensive reagents and involves only available *peri*-diaminonaphthalenes **7**. We failed to perform alkylation of 6-amino-2,2-dimethyl-2,3-dihydroperimidine and to obtain dimethylamino derivative **11** because the former compound is highly labile and is readily oxidized, both properties being more pronounced than those exhibited by 1,4,5-triaminonaphthalene. However, these reactions with the use of 1,8-diamino-3-nitronaphthalene (**7**, R = 3-NO_2) afforded very rare 5-R-perimidine representatives **9**.[14]

Exhaustive methylation of aromatic amines with solutions of formaldehyde in the presence of $NaBH_4$ can be used as an alternative to the reaction **8** → **3** involving MeI.[15] We found that in the case of dihydroperimidines **8**, the former procedure is highly competitive with the reaction using MeI in efficiency and the nitro group remained intact under the action of the reducing agent present in the reaction medium. In addition, this procedure presents yet another unique possibility.[15] It appeared that reductive alkylation of diamines **7**, as such, instead of compounds **8** afforded 1,3-dimethyl-2,3-dihydroperimidines **13** rather than the expected 1,8-bis(dimethylamino)naphthalenes **12**.



12



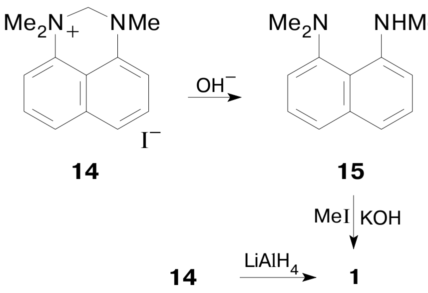
13

Apparently, formaldehyde in these reactions acted simultaneously as the alkylating and cyclization agent. This procedure is the best one of all known methods for the synthesis of 1,3-dimethyl-2,3-dihydroperimidines.[16,17] For example, the reaction of 1,8-diaminonaphthalene afforded dihydroperimidine **13** (R = H, the yield was higher than 90%) in one step and the reaction of 1,8-diamino-3-nitronaphthalene (**7**, R = 3-NO_2) gave rise to compound **13** (R = 5-NO_2) in ~35% yield. We found that under these conditions, 1,5-diaminonaphthalene and *o*-phenylenediamine underwent only alkylation to form exclusively bis(dimethylamino) derivatives in 80—90% yields.

The previously unknown 1,1,2,2,3-pentamethyl-2,3-dihydroperimidinium iodide (**4**) was prepared by heating a mixture of compound **3** and MeI in DMF (70 °C, 4 h). However, treatment of the crystals that precipitated with a solution of alkali unexpectedly afforded 1,8-bis(dimethylamino)naphthalene (**1**, the yield was ~95%), and the crystals appeared to be hydroiodide of the latter compound. Apparently, salt **4** that formed in the first step underwent further transformations under the reaction conditions.

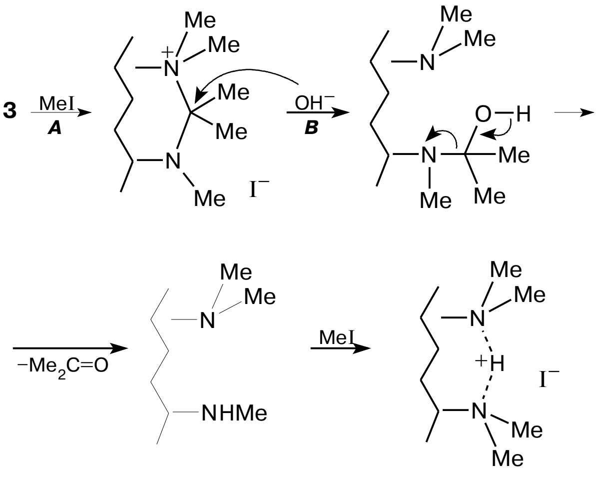
Previously,[18] it has been demonstrated that 1,1,3-trimethyl-2,3-dihydroperimidinium iodide (**14**) can be reduced with $LiAlH_4$ immediately to 1,8-bis(dimethylamino)naphthalene (**1**), whereas treatment of **14** with an aqueous solution of alkali afforded 1,8-diamino-*N*,*N*,*N'*-trimethylnaphthalene (**15**) in high yield. The latter was also readily converted into compound **1** (Scheme 3).

Scheme 3



Apparently, water, which was initially present as an impurity in DMF, acted as a nucleophile in the reaction with salt **4** giving rise to acetone and hydroiodic acid as by-products. The resulting diamine **15** readily underwent quaternization in the presence of an excess of MeI to give finally hydroiodide of "proton sponge" **1** (Scheme 4, Table 1).

Scheme 4



This scheme is supported by the following facts:

a) the reaction was substantially accelerated in the presence of KOH;

Table 1. Reaction conditions for 1,2,2,3-tetramethyl-2,3-dihydroperimidine (**3**) with MeI

Reagent	Reaction conditions	τ/h[a]	Products[b] (%)	
			1 · HI	**4**
MeI[c]	70 °C	4	95	0
MeI (moist)[d]	Refluxing	6	78	22
MeI (moist)	Refluxing	12	100	0
MeI (dried with P_2O_5)	Refluxing	6	48	52
MeI (anhydr.), **3** dried *in vacuo*[e]	Refluxing	6	0	100

[a] The reaction time.

[b] According to the ^1H NMR spectral data.

[c] In the presence of DMF.

[d] The degrees of conversion of **3** upon heating in MeI were 22% (1 h), 71% (3 h), and 100% (6 h).

[e] The solution was protected with a tube containing $CaCl_2$.

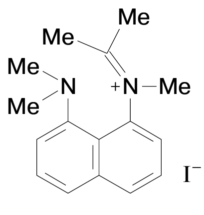
b) salt **4** can be isolated in individual form upon refluxing of compound **3** in anhydrous MeI (see Table 1);

c) heating of salt **4** with an aqueous solution of alkali afforded diamine **15**;

d) heating of salt **4** in moist DMF or in water gave rise to hydroiodide of trimethyl derivative **15**.

As can be seen from Table 1, the ratio between the salts formed (**1 · HI** and **4**) depends essentially on the reaction conditions. Eventually, salt **4** can be completely and irreversibly converted into hydroiodide of "proton sponge" **1** in the presence of water, particularly, in the case of a large reaction time.

We found that salt **4**, unlike salt **14**, is hydrolytically unstable due to its structural features. According to the data from ^1H NMR spectroscopy (CD_3CN), this compound exists in solutions exclusively as acyclic iminium cation **4a**.



4a

Actually, the NMR spectrum of cation **14** has a six-proton signal of the methyl groups bound to the onium nitrogen atom at substantially lower field (δ 3.58, CD_3CN, see the Experimental section) compared to the three-proton singlet of the Me group bound to the uncharged nitrogen atom (δ 3.35). Evidently, if salt **4** existed in the cyclic form, an analogous regularity would be observed for this salt as well. However, the ^1H NMR spectrum of salt **4** has a three-proton signal at lower field (δ 3.68), whereas the signals for two methyl groups of the NMe_2 fragment are observed at δ 3.26 and 3.28. Judging from the chemical shifts of these signals, the positive charge in the cation of this salt, like that in cation **4a**, is located predominantly on the imonium fragment =N—Me rather than on the NMe_2 group, as in structure **4**.

Interestingly, all five methyl groups in the spectrum of this salt are magnetically nonequivalent and give individual signals. The difference in the chemical shifts is particularly large for the signals of the methyl protons involved in the isopropylidene group (δ ~0.8), which is, apparently, associated with their *cis,trans* arrangement and with the different anisotropic effect of the naphthalene ring. Heating of the solution up to 80 °C did not lead to coalescence of the signals.

Unfortunately, although salt **4a** was crystallized from anhydrous MeCN, it was slowly hydrolyzed even at ~20 °C, which did not allow us to perform X-ray diffraction analysis of this salt. The course of hydrolysis can be followed directly by ^{1}H NMR spectroscopy in CD_3CN. Thus, the signal of water present in the solvent completely disappeared after several hours; instead, new peaks corresponding to acetone and hydroiodide of compound **15** appeared, which confirms the proposed sequence of conversions of salt **4a**.

Salt **4a** was hydrolyzed in DMSO even in the process of dissolution due to high basicity of the solvent, whereas this salt in anhydrous MeCN or under other anhydrous conditions can exist indefinitely.

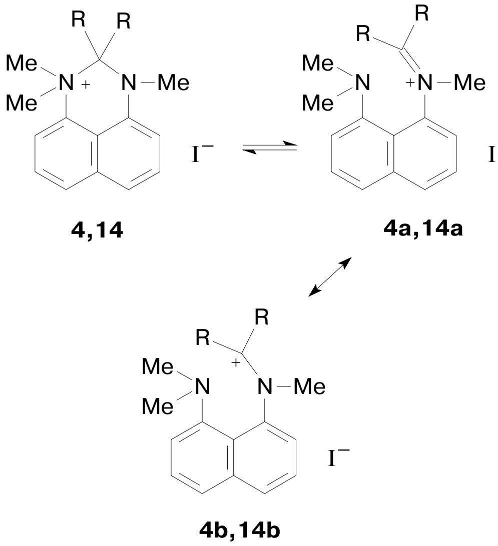
We found that melting of compounds **4a** and **14** was accompanied by vigorous decomposition into the initial components with elimination of MeI. Previously, it has been postulated that iminium cations can be formed as probable intermediates in the synthesis of some "proton sponges" and dehydroperimidines.[15,19] However, these cations have not yet been isolated and characterized.

It is of interest to elucidate the question of whether the conversion of unsubstituted tetramethyldihydroperimidine **3** into 1,8-bis(dimethylamino)naphthalene (**1**) is a common process. Apparently, this conversion should be hindered if the naphthalene ring in compound **3** bears electron-withdrawing substituents, which inhibit the quaternization stage ***A*** by decreasing the basicity of the N atoms in the heterocycle (see Scheme 4). This stage is often reversible and the subsequent reaction of acceptor-containing quaternary salts with nucleophiles (stage ***B***) proceeds anomalously.[20] Actually, there were no indications that the reactions proceeded upon prolonged heating of dihydroperimidines **9** and **10** as well as of the derivative with R = 4-CHO [21] in the MeI—DMF mixture. The addition of alkali led to gradual resinification of the starting compounds.

To the contrary, the presence of electron-donating substituents in the naphthalene ring should be favorable for the stage ***A*** and slow down the attack of the nucleophile on the *meso*-carbon atom at the stage ***B*** (see Scheme 4). Although we did not have dimethylamino derivative **11** at our disposal, we succeeded in converting dihydroperimidine **8** (R = 6-NH_2) into the corresponding "proton sponge" upon heating in the MeI—K_2CO_3—MeOH system. 1,4,5-Tris(dimethylamino)naphthalene (**12**, R = 4-NMe_2) was obtained in a yield of higher than 50%. This indicates that Scheme 4 is completely realized in the case of R = 6-NMe_2, as in the case of R = H.

Taking into account the low basicity of 1,3-dimethyl-2,3-dihydroperimidines (**13**) compared to their 2-Alk-containing analogs (for example, the pK_a values for compounds **13** (R = H) and **3** in MeCN are 8.67 and 10.51, respectively[22]), the rate of decomposition of salts **14** would be expected to be higher than the corresponding rate for compound **4**. However, it is known[17] that heating of dihydroperimidine **13** (R = H) with MeI in DMF (100 °C, 2 h) afforded methoiodide **14** in high yield rather than hydroiodide of compound **1**. Probably, the S_N1 mechanism associated with the high stability of the acyclic form of the iminium salt, which resonates between structures **4a** and **4b** (Scheme 5) and is readily subjected to the nucleophilic attack, plays a particular role in the reactions presented in Scheme 4. To the contrary, it is unlikely that such stability is characteristic of structures **14a** and **14b** derived from hydrolytically stable iodide **14** (the latter can be crystallized from water or alcohol[17]), which exists exclusively in the cyclic form.

Scheme 5

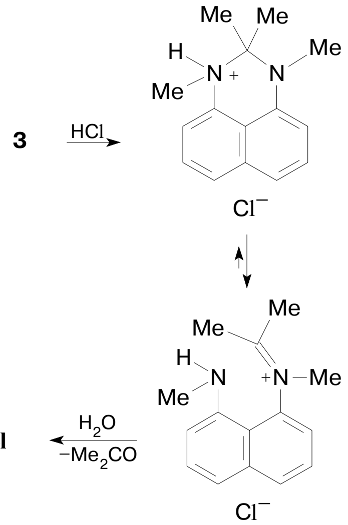


R = Me (**4**, **4a**, **4b**), H (**14**, **14a**, **14b**)

In our opinion, steric hindrance caused by the forced proximity of four methyl groups makes the major contribution to the stability of the acyclic form of salt **4**. Such steric hindrance is absent in forms **4a,b**. This is indirect evidence that the pyrimidine-ring opening in dihydroperimidine **3** can be caused not only by its quaternization under the action of MeI, but also by protonation under the action of acids.

Due to rather high basicity, compound **3** is readily dissolved in 20% HCl or 46% HBr at ~20 °C and can be readily recovered from the solutions under the action of ammonia or alkalis. However, heating of acidic solutions gave radically different results. Refluxing of 1,2,2,3-tetramethyl-2,3-dihydroperimidine in 20% HCl over a short period (5 min) led to its conversion into 1,8-bis(methylamino)naphthalene (**6**) (40%, as hydrochloride). The latter was obtained in quantitative yield when the reaction time was increased to 1 h. Evidently, this overall process also involved iminium salt of type **4a** and can be described by Scheme 6.

Scheme 6



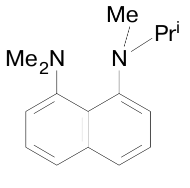
Apparently, 1,8-diamino-*N*,*N′*-dimethylnaphthalenes containing substituents in the naphthalene ring can also be synthesized in a similar way using the corresponding tetramethyl derivatives. However, this possibility was not examined in the present study. Dihydroperimidine **13** (R = H) underwent no conversions upon heating in acids.

Interestingly, elimination of the *meso*-isopropylidene group occurred even in the case of 2,2-dimethyl-2,3-dihydroperimidine. However, the latter has lower ability to undergo protonation compared to compound **3** due to which concentrated solutions of mineral acids and a higher reaction temperature are required. Thus, refluxing of dihydroperimidine **8** (R = H) in 46% HBr for 1.5 h followed by alkalization afforded 1,8-diaminonaphthalene in 97% yield.

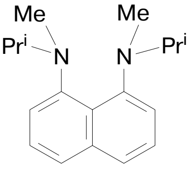
The fact that the hydrocarbon bridge in dihydroperimidines **8** is rather readily removed under the action of acids can be used for synthetic purposes. For example, recyclization can be performed in the presence of other cyclization agents. Thus, heating of a mixture of HBr and 2,2-dimethyl-2,3-dihydroperimidine in the presence of even a small amount of HCOOH afforded perimidine **16** (Scheme 7). The formation of perimidine in pure HCOOH did not occur, but this compound was formed in the presence of several drops of concentrated HBr.

As mentioned above, "proton sponges" **12** can be synthesized by reduction of quaternary 2,3-dihydroperimidinium salts. We found that salt **4a** was smoothly converted into 1,8-diamino-*N*-isopropyl-*N*,*N′*,*N′*-trimethylnaphthalene (**17**) under the action of $NaBH_4$. The reaction can be performed in EtOH or MeCN, it is exothermic and is completed in 5 min, which allows one to use moist solvents. Compound **17** was also prepared by the independent synthesis upon heating of diamine **15** with isopropyl bromide (the yield was 90%).

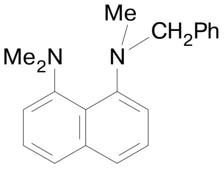
Therefore, the previously unknown *N*-isopropyl-containing "proton sponges" can be synthesized with the use of quaternary salts derived from compound **4**. However, heating of tetramethyl derivative **3** in Pr^iBr or in the Pr^iBr—DMF system containing traces of water did not give rise to hydrobromide of compound **18**. The latter would be expected to be formed according to Scheme 4; instead, the initial dihydroperimidine was completely regenerated. Apparently, the reaction did not proceed due to high steric requirements imposed on the reaction in the first stage of quaternization.



17



18



19

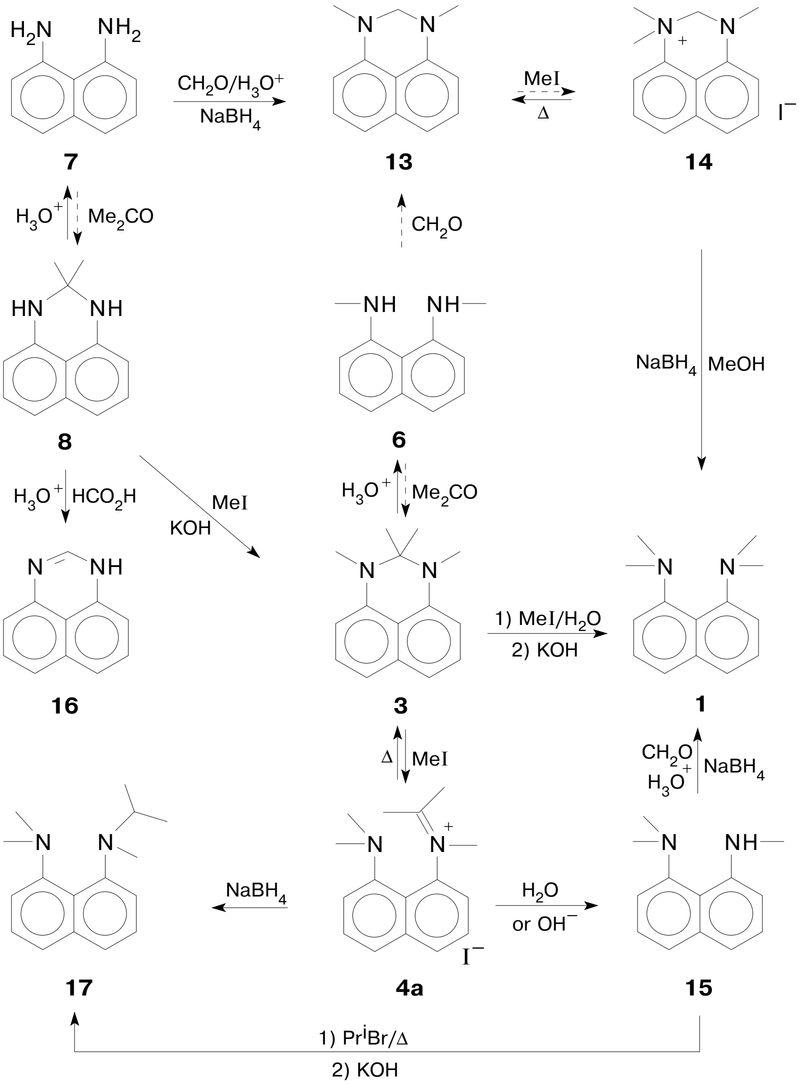
It should be noted that the ^1H NMR spectrum of compound **17** in $CDCl_3$ at ~20 °C has individual signals for the methyl protons of the 8-NMe_2 group, which coalesce at 40 °C. This corresponds to the activation energy $\Delta G^{\neq} \approx 65$ kJ mol^{-1}. The nature of an analogous conformational transition has been discussed previously.[23] It was mentioned that the methyl groups of the NMe_2 fragment in benzyl derivative **19** become magnetically nonequivalent only at −38 °C ($\Delta G^{\neq} = 57$ kJ mol^{-1}), whereas these groups in 1,8-bis(dimethylamino)naphthalene become nonequivalent only at −120 °C ($\Delta G^{\neq} = 31$ kJ mol^{-1}).

At high temperature (56 °C), the signals of the CMe_2 fragment of "proton sponge" **17** coalesce, whereas these signals at 25 °C are observed as two doublets. Based on this fact, we estimated the barrier to rotation of the isopropyl group in molecule **17** about the N—C bond ($\Delta G^{\neq} \approx 67$ kJ mol^{-1}).

Due to the stronger +*I* effect of the $CHMe_2$ group compared to that of the Me group, the presence of the former in compound **17** should lead to an increase in the basicity of this compound. Actually, the pK_a value measured by us for derivative **17** in DMSO at ~20 °C is 7.6 compared to 7.5 for 1,8-bis(dimethylamino)naphthalene.[24]

In conclusion, it is worthwhile to give the general scheme of interconversions between 2,3-dihydroperimidines, 1,8-diaminonaphthalenes, and "proton sponges" most of which were found and performed in the present study (see Scheme 7). The conversions indicated in the scheme by dashed arrows have been described previously: **6** → **3**,[11] **7** → **8**,[12] **13** → **14**,[17] and **6** → **13**.[19]

Scheme 7



Experimental

The ^{1}H NMR spectra were measured on a Bruker DPX-250 instrument (250 MHz) in $CDCl_3$ with Me_4Si as the internal standard. The IR spectra were recorded on a Specord IR-71 spectrometer in Nujol mulls. The purities of the compounds were monitored by TLC on Al_2O_3 (Brockmann III) and Silufol plates using $CHCl_3$ as the eluent; visualization was carried out with iodine vapor.

1,8-Diaminonaphthalenes 7 were prepared according to known procedures (R = 3-NO_2, 4-NO_2,[14] and 4-NH_2[25]). Unsubstituted 1,8-diaminonaphthalene (97%) was purchased from Aldrich.

Other reagents and solvents were purified and dried according to standard procedures.[27]

1,4,5-Triaminonaphthalene (7, R = 4-NH_2). ^{1}H NMR, δ: 4.10 (br.s, 6 H, 3 NH_2); 6.50 (d, 1 H, H(3), $J_{2,3}$ = 7.8 Hz); 6.58 (m, 2 H, H(2), H(6)); 7.15 (d, 1 H, H(8), $J_{7,8}$ = 7.4 Hz); 7.19 (t, 1 H, H(7), $J_{6,7}$ = 8.4 Hz). IR, ν/cm^{-1}: 3440, 3390, 3340, 3290, 3200 (NH_2); 1600, 1580, 1515 (ring).

2,2-Dimethyl-2,3-dihydroperimidines 8 were prepared by dissolution of the corresponding diamines **7** in acetone and filtration of the resulting solutions of perimidines **8** through a layer of Al_2O_3 using acetone as the eluent.[12] The movement of colorless compounds **8** (R = H or 6-NH_2) along the sorbent was monitored with an UV lamp (violet or blue light). The complete conversion of low-basicity diamine **7** (R = 4-NO_2) into the cyclization product required refluxing in acetone over a short period. Compounds **8** were obtained in virtually 100% yields.

2,2-Dimethyl-2,3-dihydroperimidine (8, R = H). M.p. and the IR spectrum correspond to the published data.[12] ^{1}H NMR, δ: 1.48 (s, 6 H, CMe_2); 4.15 (br.s, 2 H, 2 NH); 6.45 (dd, 2 H, H(4), H(9), $J_{4,5}$ = 7.2 Hz); 7.13 (dd, 2 H, H(6), H(7), $J_{4,6}$ = 0.9 Hz); 7.22 (t, 2 H, H(5), H(8), $J_{5,6}$ = 8.2 Hz).

2,2-Dimethyl-6-nitro-2,3-dihydroperimidine (8, R = 6-NO_2). Red crystals, m.p. 135 °C (from 95% EtOH). Found (%): C, 64.07; H, 5.46. $C_{13}H_{13}N_3O_2$. Calculated (%): C, 64.19; H, 5.39. ^{1}H NMR, δ: 1.52 (s, 6 H, CMe_2); 5.97 (br.s, 2 H, 2 NH); 6.32 and 6.56 (both d, 1 H each, H(4), H(9), $J_{4,5}$ = 8.7 Hz, $J_{8,9}$ = 7.5 Hz); 7.47 (t, 1 H, H(8), $J_{7,8}$ = 8.9 Hz); 8.33 and 8.41 (both d, 1 H each, H(7), H(5)). IR, ν/cm^{-1}: 3325, 3200 (NH); 1530, 1350 (NO_2).

6-Amino-2,2-dimethyl-2,3-dihydroperimidine (8, R = 6-NH_2). A dark-grey compound, which rapidly turns dark in air and in solutions and which does not possess the exact melting point. Found (%): C, 73.30; H, 7.14. $C_{13}H_{15}N_3$. Calculated (%): C, 73.21; H, 7.09. ^{1}H NMR, δ: 1.45 (s, 6 H, CMe_2); 3.5 (br.s, 2 H, NH_2); 4.15 (br.s, 2 H, 2 NH); 6.41 and 6.49 (both d, 1 H each, H(4), H(9), $J_{4,5}$ = 7.7 Hz, $J_{8,9}$ = 7.4 Hz); 6.63 and 7.12 (both d, 1 H each, H(5), H(7), $J_{7,8}$ = 8.3 Hz); 7.24 (t, 1 H, H(8)). IR ($CHCl_3$), ν/cm^{-1}: 3390, 3330, 3280 (NH).

1,2,2,3-Tetramethyl-2,3-dihydroperimidines (general procedure). Ground KOH (0.224 g, 4 mmol) was added to a solution of dihydroperimidine **8** (1 mmol) in DMF (2 mL) and then MeI (0.25 mL, 4 mmol) was added in one portion with stirring. The reaction mixture was heated at 75—85 °C, stirred during the required time (see below), diluted by a factor of three with water without cooling, and extracted with hot *n*-hexane (4×10 mL). The hexane was removed and the residue was crystallized from a suitable solvent or chromatographed on silica gel (Aldrich, 70—230 mesh, 60 Å, $CHCl_3$ as the eluent).

1,2,2,3-Tetramethyl-2,3-dihydroperimidine (3). The time of heating was 50 min. The yield was 90%. The properties of the compound are identical with those reported in the literature.[10] ^{1}H NMR, δ: 1.39 and 2.94 (both s, 6 H each, CMe_2, 2 NMe); 6.59 (dd, 2 H, H(4), H(9), $J_{4,5}$ = 7.6 Hz); 7.19 (dd, 2 H, H(6), H(7), $J_{4,6}$ = 0.9 Hz); 7.31 (t, 2 H, H(5), H(8), $J_{5,6}$ = 8.5 Hz).

1,2,2,3-Tetramethyl-5-nitro-2,3-dihydroperimidine (9). The time of heating was 1 h. The yield was 80%. Brick-red crystals, m.p. 122—123 °C (from 95% EtOH). Found (%): C, 66.54; H, 6.28. $C_{15}H_{17}N_3O_2$. Calculated (%): C, 66.40; H, 6.32. ^{1}H NMR, δ: 1.34 (s, 6 H, CMe_2); 2.87 and 2.95 (both s, 3 H each, C(1)NMe and C(3)NMe); 6.65 (br.d, 1 H, H(9), $J_{8,9}$ = 8.4 Hz); 7.11 (d, 1 H, H(4), $J_{4,6}$ = 2.1 Hz); 7.33 (t, 1 H, H(8), $J_{7,8}$ = 7.9 Hz); 7.78 and 7.97 (both d, 1 H each, H(7), H(6)).

1,2,2,3-Tetramethyl-6-nitro-2,3-dihydroperimidine (10). The time of heating was 1.5 h. The yield was 75%. Needle-like cherry-red crystals, m.p. 161—162 °C (from 95% EtOH). Found (%): C, 66.47; H, 6.24. $C_{15}H_{17}N_3O_2$. Calculated (%): C, 66.40; H, 6.32. ^{1}H NMR, δ: 1.38 (s, 6 H, CMe_2); 2.84 and 3.01 (both s, 3 H each, C(1)NMe and C(3)NMe); 6.32 (d, 1 H, H(4), $J_{4,5}$ = 9.1 Hz); 6.64 (br.d, 1 H, H(9), $J_{8,9}$ = 8.0 Hz); 7.45 (dd, 1 H, H(8), $J_{7,8}$ = 8.8 Hz); 8.33 and 8.34 (both d, 1 H each, H(7), H(5), $J_{7,9}$ = 0.5 Hz).

1,3-Dimethyl-2,3-dihydroperimidines 13 were prepared according to a procedure reported previously[15] from the corresponding 1,8-diaminonaphthalenes. The use of this procedure in the case of trimethyl derivative **15** in the presence of a formaldehyde solution and $NaBH_4$ taken in amounts four times larger than those reported in the literature[15] made it possible to obtain 1,8-bis(dimethylamino)naphthalene (**1**) in a yield of up to 78% (see Scheme 7).

1,3-Dimethyl-2,3-dihydroperimidine (13, R = H). The yield was 93%. The properties of the compound are identical with those published in the literature.[16,17] ^{1}H NMR, δ: 3.03 (s, 6 H, 2 NMe); 4.18 (s, 2 H, CH_2); 6.55 (dd, 2 H, H(4), H(9), $J_{4,5}$ = 7.7 Hz); 7.23 (dd, 2 H, H(6), H(7), $J_{4,6}$ = 0.9 Hz); 7.35 (t, 2 H, H(5), H(8), $J_{5,6}$ = 8.4 Hz).

1,3-Dimethyl-5-nitro-2,3-dihydroperimidine (13, R = 5-NO_2). The yield was 33%. Red crystals, m.p. 125—127 °C (from *n*-hexane). Found (%): C, 64.53; H, 5.47. $C_{13}H_{13}N_3O_2$. Calculated (%): C, 64.19; H, 5.39. ^{1}H NMR, δ: 3.01 and 3.07 (both s, 3 H each, C(1)NMe and C(3)NMe); 4.22 (s, 2 H, CH_2); 6.68 and 7.16 (both d, 1 H each, H(9), H(4), $J_{4,6}$ = 2.2 Hz, $J_{8,9}$ = 7.8 Hz); 7.33 (d, 1 H, H(7), $J_{7,8}$ = 8.1 Hz); 7.44 (t, 1 H, H(8)); 8.10 (d, 1 H, H(6)).

1,1,3-Trimethyl-2,3-dihydroperimidinium iodide (14) was prepared from compound **13** (R = H) according to a procedure reported previously.[17] ^{1}H NMR (CD_3CN), δ: 3.35 (s, 3 H, C(3)NMe); 3.58 (br.s, 6 H, C(1)NMe_2); 4.97 (br.s, 2 H, H(2)); 7.07 and 7.59 (both dd, 1 H each, H(4), H(6), $J_{4,5}$ = 7.4 Hz, $J_{5,6}$ = 8.2 Hz, $J_{4,6}$ = 1.1 Hz); 7.66 (m, 2 H, H(5), H(8)); 7.86 and 8.07 (both br.d, 1 H each, H(9), H(7), $J_{8,9}$ = 7.7 Hz, $J_{7,8}$ = 8.3 Hz).

Salt 4 was prepared from dihydroperimidine **3** (0.5 mmol) and MeI (2 mL) (see Table 1). The iodomethane was removed and the crystals were washed three times with anhydrous ether. Compound **4** was obtained as bright yellowish-brown crystals, m.p. 147—148 °C (from anhydrous MeCN). It decomposed on melting to form the initial components. Found (%): C, 52.01; H, 6.10; I, 35.33. $C_{16}H_{21}IN_2$. Calculated (%): C, 52.18; H, 5.75; I, 34.46. ^{1}H NMR (CD_3CN), δ: 1.34 and 2.11 (both s, 3 H each, CMe_2); 3.26 and 3.28 (both s, 3 H each, C(8)NMe_2); 3.68 (s, 3 H, C(1)NMe); 7.17 and 7.62 (both dd, 1 H each, H(7), H(5), $J_{5,7}$ = 1.3 Hz, $J_{6,7}$ = 7.3 Hz); 7.67 (m, 2 H, H(3), H(6)); 7.96 and 8.08 (both d, 1 H each, H(2), H(4), $J_{2,3}$ = 7.6 Hz, $J_{3,4}$ = 8.4 Hz).

1,8-Diamino-*N*,*N*,*N*′-trimethylnaphthalene (15) was obtained as hydroiodide in quantitative yield upon heating of salt **4** (0.5 mmol) in water or another moist solvent (MeCN, alcohol, or DMF) (2 mL) for 5—10 min. Alkalization of the solution afforded free base **15** as a colorless oil readily soluble in dilute mineral acids.[18] Hydroiodide **15 · HI** existed as needle-like yellowish crystals (from MeCN), t.decomp. 170 °C; it deliquesces in air. Found (%): C, 47.39; H, 5.35; I, 39.22. $C_{13}H_{17}IN_2$. Calculated (%): C, 47.58; H, 5.22; I, 38.67. ^{1}H NMR, (CD_3CN), δ: 2.99 (s, 6 H, C(1)NMe_2); 3.07 (s, 3 H, C(8)NMe); 7.67 (m, 2 H, H(3), H(6)); 7.78 (dd, 1 H, H(7), $J_{6,7}$ = 7.5 Hz, $J_{5,7}$ = 1.2 Hz); 7.85 (dd, 1 H, H(2), $J_{2,3}$ = 7.6 Hz, $J_{2,4}$ = 1.0 Hz); 8.01 (m, 2 H, H(4), H(5), $J_{3,4}$ = 8.1 Hz, $J_{5,6}$ = 8.0 Hz); 12.6 (br.s, 2 H, NH).

1,8-Bis(methylamino)naphthalene (6). A solution of dihydroperimidine **3** (0.1 mmol) in 20% HCl (2 mL) was refluxed for 1 h. Then the reaction mixture was cooled, neutralized with a 10% solution of KOH, and extracted with *n*-hexane. Chromatographically pure diamine **6** was obtained in quantitative yield as colorless crystals, m.p. 102—103 °C.[22]

1,8-Diaminonaphthalene (7, R = H). A suspension of dihydroperimidine (**8**, R = H) (0.1 mmol) in 46% HBr (2 mL) was refluxed for 1.5 h. Then the reaction mixture was cooled, neutralized with a 10% solution of KOH, and extracted with *n*-hexane. Diamine **7** was obtained in quantitative yield; its properties are identical with those of the authentic sample.

Perimidine 16 (see Scheme 7). A mixture of dihydroperimidine **8** (R = H) (0.1 mmol), 85% HCOOH (0.5 mL), and 46% HBr (1.5 mL) was refluxed for 1.5 h. Then the yellow-brown solution was cooled and neutralized with concentrated NH_3 until a persistent odor appeared. The yellow-green precipitate of perimidine that formed was filtered off, washed with water, and dried in air. The yield was 97%, m.p. 223—224 °C.[26]

1,8-Bis(dimethylamino)naphthalenes (12). Iodomethane (2 mL) was added to a solution of dihydroperimidine **3** (0.1 mmol) in DMF (5 mL). Then the reaction mixture was stirred at 70 °C for 4 h and diluted with an equal amount of ether. Hydroiodide of diamine **1** that formed was filtered off and decomposed with a 20% solution of KOH. After extraction with *n*-hexane and removal of the solvent, **1,8-bis(dimethylamino)naphthalene (1)** was obtained in 95% yield as virtually colorless crystals, m.p. 47—48 °C.[18] The use of salt **4** or trimethyl derivative **15** instead of compound **3** gave an analogous result. The same "proton sponge" can be prepared by reduction of quaternary salt **14** with $NaBH_4$ in aqueous alcohol, aqueous THF, or MeOH (in all cases, the yields were higher than 90%, see Scheme 7).

The application of this procedure to dihydroperimidine **8** (R = 6-NH_2) with the use of MeOH instead of DMF in the presence of K_2CO_3 (0.8 mmol) afforded **1,4,5-tris(dimethylamino)naphthalene 12** (R = 4-NMe_2) as a reddish oil in 50—55% yield. The physicochemical characteristics of this "proton sponge" are identical with those of the specimen prepared previously.[24]

1,8-Diamino-*N*-isopropyl-*N*,*N′*,*N′*-trimethylnaphthalene (17). ***A***. Dispersed $NaBH_4$ (8 mg, 0.2 mmol) was suspended in MeCN (1 mL) for 1 min. Then salt **4** (74 mg, 0.2 mmol) was added in one portion with vigorous stirring and cooling with water (the mixture warmed up). After stirring for 5 min, the mixture was diluted with an equal amount of water. The oil that formed was extracted with *n*-hexane. After removal of the solvent, compound **17** was obtained as a virtually colorless oil readily soluble in dilute mineral acids. The yield was 95—97%. Found (%): C, 79.56; H, 8.99. $C_{16}H_{22}N_2$. Calculated (%): C, 79.29; H, 9.15. ^1H NMR (25 °C), δ: 0.62 and 1.24 (both d, 3 H each, CMe_2, $J_{CH,Me}$ = 6.3 Hz); 2.65 and 2.85 (both br.s, 3 H each, C(8)NMe_2); 2.79 (s, 3 H, C(1)NMe); 3.50 (m, 1 H, —CH<); 6.90 and 6.97 (both br.d, 1 H each, H(2), H(7), $J_{2,3}$ = 7.3 Hz, $J_{6,7}$ = 7.4 Hz); 7.27 (m, 2 H, H(3), H(6)); 7.30 (m, 2 H, H(4), H(5)). ^1H NMR (56 °C), δ: 1.00 (br.s, 6 H, CMe_2); 2.77 (s, 6 H, C(8)NMe_2); 2.81 (s, 3 H, C(1)NMe); 3.54 (septet, 1 H, —CH<, $J_{CH,Me}$ = 6.6 Hz); 6.92 and 6.99 (both br.d, 1 H each, H(2), H(7), $J_{2,3}$ = 7.14 Hz, $J_{6,7}$ = 7.13 Hz); 7.27 (m, 2 H, H(3), H(6)); 7.36 (m, 2 H, H(4), H(5)). Perchlorate **17 · $HClO_4$**: colorless crystals, m.p. 198—200 °C (with decomp., from 95% EtOH). Found (%): C, 55.82; H, 6.94; Cl, 10.80. $C_{16}H_{23}ClN_2O_4$. Calculated (%): C, 56.06; H, 6.76; Cl, 10.34. ^1H NMR (DMSO-d_6), δ: 0.93 and 1.43 (both d, 3 H each, CMe_2, $J_{CH,Me}$ = 6.4 Hz); 3.07 and 3.12 (both br.d, 3 H each, C(8)NMe_2, $J_{NH,C(8)NMe}$ = 2.1 Hz); 3.24 (d, 3 H, C(1)NMe, $J_{NH,C(1)NMe}$ = 2.7 Hz); 3.76 (m, 1 H, —CH<); 7.76 (m, 2 H, H(3), H(6)); 8.09 (m, 4 H, H(2), H(4), H(5), H(7)); 17.96 (br.s, 1 H, NH).

Reduction can be performed in MeOH. In this case, salt **4** was introduced immediately after the addition of dispersed $NaBH_4$. The reaction mixture was stirred for 5 min and diaminonaphthalene **17** was isolated as described above.

B. A solution of trimethyl derivative **15** (0.1 mmol) was refluxed in Pr^iBr (3 mL) for 36 h. After cooling of the reaction mixture, the hydrobromic salt that eliminated (m.p. 202—203 °C, with decomp.) was separated, washed with ether, and decomposed with a 10% solution of KOH on heating to 100 °C. The oil that formed was extracted and compound **17** was isolated as described in procedure ***A***. The yield was 90%. The physicochemical characteristics of the compound are analogous to those of the sample prepared according to procedure ***A***.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 99-03-33133a).

References

1. V. A. Ozeryanskii and A. F. Pozharskii, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 1412 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 1406].
2. N. V. Vistorobskii and A. F. Pozharskii, *Zh. Org. Khim.*, 1989, **25**, 2154 [*Russ. J. Org. Chem.*, 1989, **25** (Engl. Transl.)].
3. L. Maresca, G. Natile, and F. P. Fanizzi, *J. Chem. Soc., Dalton Trans.*, 1992, **11**, 1867.
4. A. F. Pozharskii, *Usp. Khim.*, 1998, 67, 3 [*Russ. Chem. Rev.*, 1998, **67**, 1 (Engl. Transl.)].
5. N. V. Vistorobskii, A. F. Pozharskii, S. V. Shorshnev, and A. I. Chernyshev, *Mendeleev Commun.*, 1991, 10.
6. A. F. Pozharskii, N. G. Tregub, N. V. Vistorobskii, E. Yu. Romanova, Z. A. Starikova, and A. I. Yanovskii, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 1311 [*Russ. Chem. Bull.*, 1999, **48**, 1299 (Engl. Transl.)].
7. A. F. Pozharskii, A. N. Suslov, and V. A. Kataev, *Dokl. Akad. Nauk SSSR,* 1977, **234**, 841 [*Dokl. Chem.*, 1977 (Engl. Transl.)].
8. A. A. Espenbetov, A. F. Pozharskii, Yu. T. Struchkov, and A. N. Suslov, *Khim. Geterotsikl. Soedin.*, 1985, 977 [*Chem. Heterocycl. Compd.,* 1985 (Engl. Transl.)].
9. T. Barth and F. A. Neugebauer, *J. Org. Chem.*, 1995, **60**, 5401.
10. A. F. Pozharskii, L. P. Smirnova, A. I. Belyashova, N. N. Zatsepina, and I. F. Tupitsyn, *Khim. Geterotsikl. Soedin.*, 1979, 961 [*Chem. Heterocycl. Compd.,* 1979 (Engl. Transl.)].
11. R. Gleiter and J. Uschmann, *J. Org. Chem.*, 1986, **51**, 370.
12. S. Bradbury, C. W. Rees, and R. C. Storr, *J. Chem. Soc., Perkin Trans. 1*, 1972, 68.
13. A. F. Pozharskii and V. V. Dal′nikovskaya, *Usp. Khim.*, 1981, **50**, 1559 [*Russ. Chem. Rev.*, 1981, **50** (Engl. Transl.)].
14. V. A. Ozeryanskii and A. F. Pozharskii, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 1405 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 1399].
15. A. G. Giumanini, G. Chiavari, M. M. Musiani, and P. Rossi, *Synthesis*, 1980, 743.
16. A. F. Pozharskii and I. S. Kashparov, *Khim. Geterotsikl. Soedin.*, 1972, 860 [*Chem. Heterocycl. Compd.,* 1972 (Engl. Transl.)].
17. V. I. Sokolov, A. F. Pozharskii, I. S. Kashparov, A. G. Ivanov, and B. I. Ardashev, *Khim. Geterotsikl. Soedin.*, 1974, 558 [*Chem. Heterocycl. Compd.,* 1974 (Engl. Transl.)].
18. A. F. Pozharskii, L. A. Kurasov, V. V. Kuz′menko, and L. L. Popova, *Zh. Org. Khim.*, 1981, **17**, 1005 [*J. Org. Chem. USSR*, 1981, **17** (Engl. Transl.)].
19. R. W. Alder, M. R. Bryce, N. C. Goode, N. Miller, and J. Owen, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2840.
20. A. F. Pozharskii, V. A. Ozeryanskii, and V. V. Kuz′menko, *Zh. Org. Khim.*, 1996, **32**, 76 [*Russ. J. Org. Chem.*, 1996, **32** (Engl. Transl.)].
21. A. F. Pozharskii, E. A. Filatova, N. V. Vistorobskii, and I. V. Borovlev, *Khim. Geterotsikl. Soedin.*, 1999, 365 [*Chem. Heterocycl. Compd.,* 1999 (Engl. Transl.)].
22. A. F. Pozharskii, A. N. Suslov, N. M. Starshikov, L. L. Popova, N. A. Klyuev, and V. A. Adanin, *Zh. Org. Khim.*, 1980, **16**, 2216 [*J. Org. Chem. USSR*, 1980, **16** (Engl. Transl.)].
23. R. W. Alder and J. E. Anderson, *J. Chem. Soc., Perkin Trans. 2*, 1973, 2086.
24. V. A. Ozeryanskii and A. F. Pozharskii, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 1501 [*Russ. Chem. Bull.*, 1997, **46**, 1437 (Engl. Transl.)].
25. J. S. Whitehurst, *J. Chem. Soc.*, 1951, 215.
26. F. Sachs, *Justus Liebigs Ann. Chem.*, 1909, **365**, 53.
27. A. J. Gordon and R. A. Ford, *The Chemist′s Companion, the Handbook of Practical Data, Techniques, and References*, J. Wiley, New York—London—Sydney—Toronto, 1972.

Received August 1, 2000;
in revised form November 24, 2000