Kinetics, mechanism, and reactivity of an activated carbon—carbon double bond in nitroxyl radicals and their diamagnetic analog in interaction with some secondary amines and polyethyleneimine

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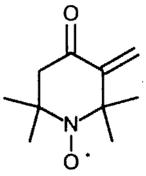
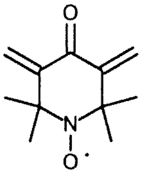
Routes for the reaction of a conjugated methylene group of nitroxyl radicals (NR) with secondary amines were suggested and analyzed. Kinetic parameters of the limiting step of this reaction for the NR—amine and diamagnetic analog of NR—amine systems were estimated. The effect of the medium on these reactions was examined. The specific behavior of polyethyleneimine in the reaction with activated methylene groups of 2,2,6,6-tetramethyl-3,5-dimethylene-4-oxopiperidine-1-oxyl was demonstrated.

Key words: unsaturated nitroxyl radicals, secondary amines, addition, kinetics, mechanism.

Reaction products of 2,2,6,6-tetramethyl-3-methylene-4-oxopiperidine-1-oxyl (**1a**) and 2,2,6,6-tetramethyl-3,5-dimethylene-4-oxopiperidine-1-oxyl (**1b**) with several secondary amines have been obtained previously[1] and characterized. The free valence was not affected in these reactions. In the present work, we performed the kinetic study of these reactions and analyzed the mechanism of the reaction of nitroxyl radicals (NR) **1a—d** with piperidine, morpholine, and polyethyleneimine (PEI).



1a



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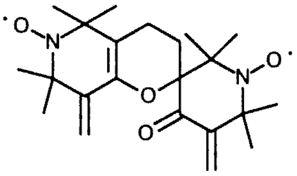
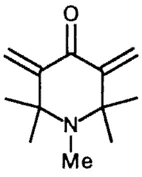


1c

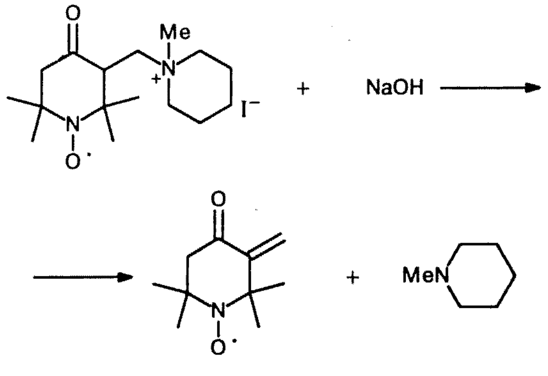


1d

Experimental

The kinetic regularities of reactions of NR with secondary amines and PEI were studied at 22 °C by the stop-flow method, using a Durrum spectrophotometer. Measurements were carried out at 270, 340, 380, and 425 nm. *n*-Hexane, toluene, chlorobenzene, *o*-dichlorobenzene, methanol and its mixtures with *n*-hexane, and mixtures of acetone with *n*-hexane were used as solvents. The concentrations of amine and PEI (5000) were 0.03 to 0.4 and 0.07 to 0.24 mol L^{-1}, respectively; the concentrations of compounds **1a—d** were $(7\text{—}40) \cdot 10^{-4}$ mol L^{-1}. The following constants of amine dimerization were used for the calculation of the monomeric form of amine[2,3]: for piperidine, 0.3 L mol^{-1} and for morpholine, 2.4 L mol^{-1}. Compounds **1b,c** were synthesized as described previously.[1]

Compound **1a** was obtained by the following reaction:



1a

A 0.1 % solution of NaOH was added to an aqueous solution of salt. The reaction was completed in less than 1 min. Compound **1a** was extracted with *n*-hexane and dried with calcium chloride and molecular sieves 4 Å. Compound **1d** was synthesized by the known procedure.[4] The dielectric permeabilities of *n*-hexane—methanol and *n*-hexane—acetone

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mixtures were calculated using the additivity rule. The effective rate constants k_{exp} of the reactions of **1a—d** with amines were calculated on a computer with a program for irreversible first-order reactions, using the time dependence of the optical density,

$$k_{\mathrm{exp}} = \frac{2.3}{\tau}\log\frac{D_0 - D_\infty}{D - D_\infty}, \qquad (1)$$

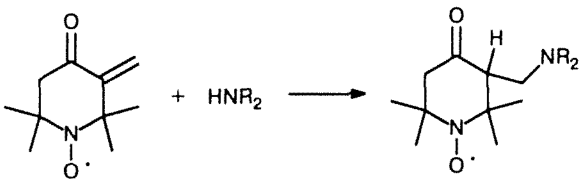
where D_0 and D are the initial and current optical densities, D_∞ is the optical density after completion of the reaction, and τ is time in sec. The error in the determination of reaction rate constants was not greater than 10—15 %.

The correlation between the real (k_1, k_2, k_3) and effective (k_{exp}) rate constants for the reactions of **1a—d** with amines is determined by Eqs. (7)—(9) (see below). Rate constants k_1, k_2, and k_3 were computed using the least-squares method.

Results and Discussion

The addition of secondary amines to the double bond activated by the carbonyl group of stable radical **1a** occurs *via* Scheme 1.

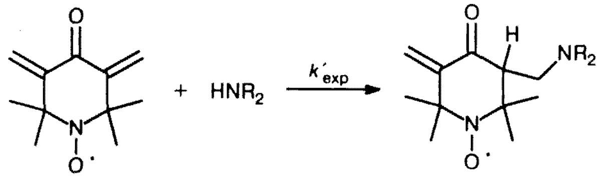
Scheme 1



1a

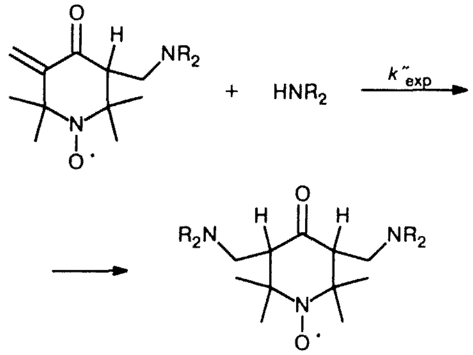
A similar reaction also occurs for **1c**, for which it is known[5] that only the double bond conjugated with the carbonyl group readily adds nucleophiles. The reaction of compound **1b** with secondary amines results in the formation of products of mono- and bis-addition *via* Schemes 2 and 3.

Scheme 2



1b

Scheme 3



As has been shown, in the reaction with piperidine (0.4 mol L^{-1}, [**1b**] = $4.7 \cdot 10^{-3}$ mol L^{-1}, 22 °C, anhydrous hexane as a solvent), the ratio of rate constants of the reactions in Schemes 2 and 3 is the following: $k'_{\mathrm{exp}}/k''_{\mathrm{exp}}$ = 0.8 s^{-1}/2 $\cdot$ 10^{-4} s^{-1} = 4 $\cdot$ 10^3. This shows that the reactions in Schemes 2 and 3 are distinctly separated in time, which allows one to measure precisely the rate constant for the reaction in Scheme 2.

In all cases, the rate of formation of the final products at a 10-fold (and higher) excess of amine obeys the regularities of irreversible first-order reactions.

The reaction order with respect to amine was determined from the logw_0 *vs.* log[$\mathbf{B}_\mathrm{M}$] dependence, where w_0 is the initial rate of the reaction in Scheme 1 or 2 determined from the consumption of compounds **1a—d**, and [$\mathbf{B}_\mathrm{M}$] is the concentration of the monomeric form of the amine. The second order with respect to amine is observed for concentrations higher than 0.1 mol L^{-1}. When the concentrations are lower than 0.1 mol L^{-1}, the reaction order decreases to the first order in all systems studied. The corresponding data for the **1c**—piperidine system are presented in Fig. 1. The reaction rate constants k_{exp} were determined by Eq. (1) for the same concentration of amine for all systems. For example, the values of [$\mathbf{B}_0$] (total concentration of amine), [$\mathbf{B}_\mathrm{M}$], [$\mathbf{B}_\mathrm{D}$] (dimeric form of amine), and k_{exp} for the **1c**—piperidine system are presented in Table 1.

Table 1. Concentrations of piperidine forms and the corresponding experimental values of the reaction rate constants of **1c** with piperidine (k_{exp}) at 22 °C in *n*-hexane

[$\mathbf{B}_0$]	[$\mathbf{B}_\mathrm{M}$]	[$\mathbf{B}_\mathrm{D}$]	k_{exp}/s^{-1}	[$\mathbf{B}_0$]	[$\mathbf{B}_\mathrm{M}$]	[$\mathbf{B}_\mathrm{D}$]	k_{exp}/s^{-1}
/mol L^{-1}				/mol L^{-1}			
0.4	0.333	0.0335	0.602	0.148	0.137	0.0055	0.132
0.333	0.285	0.0245	0.474	0.079	0.076	0.0017	0.061
0.267	0.234	0.0165	0.338	0.058	0.056	0.001	0.033
0.222	0.199	0.012	0.238	0.044	0.043	0.00055	0.025
0.178	0.162	0.008	0.183	0.029	0.0288	0.00025	0.014

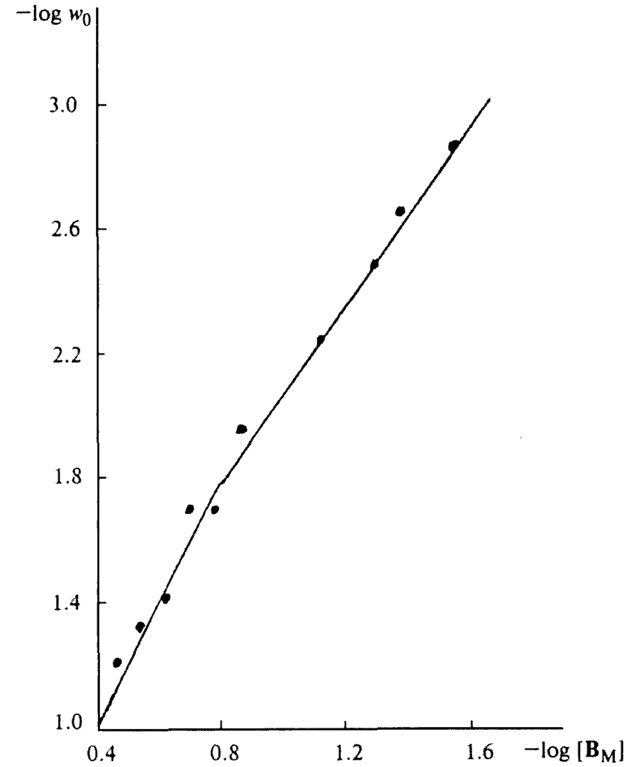


Fig. 1. Logarithmic dependence of the initial reaction rate of **1c** with piperidine on the concentration of the monomeric form of amine.

Based on the experimental results obtained and literature data,[6–11] one can suggest several routes of product formation for the reaction of conjugated enones **1a—d** with secondary amines, the most probable of which are presented below. Using compound **1a** as an example, let us consider the reaction scheme, which envisages that the amine exists in hexane in monomeric and dimeric forms, whose ratio is determined by the equilibrium constant (see Scheme 4).

Route R-1. The reaction begins from the formation of H-complex **2a** involving the carbonyl group of radical **1a** and the amine. Such complexes are known.[6–8,11] The second stage is the intramolecular nucleophilic attack by the N atom of amine on the methylene group. It is assumed that this reaction results in bipolar ion **C**, which then transforms into final product **P** *via* the enol form of ketone **D**. The possibility of generation of bipolar ions upon nucleophilic attack on the double bonds is postulated.[9] This route provides a reaction order with respect to amine of not higher than 1.

Route R-2. The reaction of H-complex **2a** with the second amine molecule, whose N atom attacks the C atom of the methylene group in **2a**, is possible along with its intramolecular transformation. This route results in the formation of the bipolar ion **C′**, which transforms stepwise into the final reaction product. The most favorable orientation of reactive groups for the intraionic proton transfer from the —N—H fragment to the carbonyl group is provided in the bipolar ion **C′** due to intramolecular H-bonds. This "relayed" proton transfer results in the formation of the enol form of ketone and release of the amine molecule.

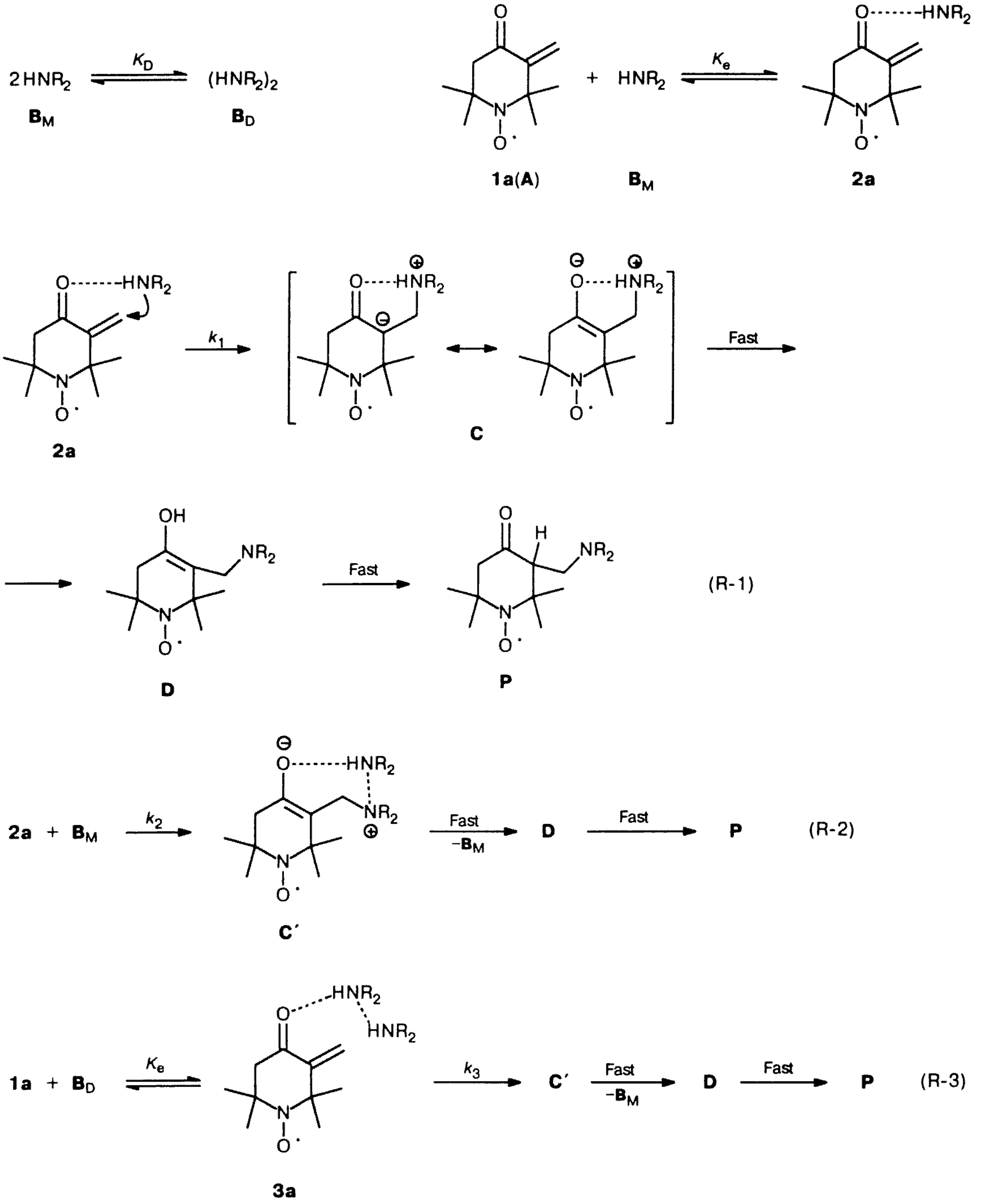
Route R-3. It should be taken into account that H-complex **3a** can be formed that involves the carbonyl group and the dimeric form of amine, whose concentration in the solution is rather high. Then the bipolar ion **C′** is formed *via* this route by the intramolecular nucleophilic attack.

The analysis of the kinetics of the reaction in Scheme 1 is based on separate consideration of routes R-1, R-2, and R-3. Assuming that the equilibrium for complex **2a** is rapidly established and its consumption with the formation of the reaction products does not disturb the equilibrium, the concentration of the complexes can be represented as follows: $[\mathbf{2a}] = K_e[\mathbf{A}][\mathbf{B}_M]$ (2); **3a**: $[\mathbf{3a}] = K'_e[\mathbf{A}][\mathbf{B}_D]$ (3), where [**A**] is the concentration of unbound form **1a**. Taking into account the mass balance, we have $[\mathbf{A}_0] = [\mathbf{A}] + [\mathbf{2a}]$ (4) for routes R-1 and R-2 and $[\mathbf{A}_0] = [\mathbf{A}] + [\mathbf{3a}]$ (5) for route R-3 under the general condition that $[\mathbf{B}_0] \gg [\mathbf{A}_0]$ (6), where $[\mathbf{B}_0]$ and $[\mathbf{A}_0]$ are the total concentrations of the amine and compounds **1a**, respectively, and [**2a**] and [**3a**] are the concentrations of H-complexes **1a** with monomeric and dimeric forms, respectively. The correlation between the experimentally determined reaction rate constant k_{exp} and kinetic and thermodynamic parameters of the reaction in Scheme 4 takes the form that is convenient for their determination. For example, for route R-1, $1/k_{exp} = 1/k_1 + 1/k_1K_e[\mathbf{B}_M]$ (7); for route R-2, $[\mathbf{B}_M]/k_{exp} = 1/k_2 + 1/k_2K_e[\mathbf{B}_M]$ (8); and for route R-3, $1/k_{exp} = 1/k_3 + 1/k_3K_e'[\mathbf{B}_D]$ (9). The stages with the rate constants k_1, k_2, and k_3 are rate-limiting,[1,9] and K_e and K_e' are the equilibrium constants of the stages of formation of H-complexes **2a** and **3a**, respectively.

Of course, one of these directions is dominating. Let us consider possible variants using as an example the **1c**—piperidine system (see Table 1). Processing of the data by Eq. (8) for the region with $n = 2$ (route R-2) gives the second-order rate constant $k_2 = 4.4$ L mol^{-1} s^{-1} and $K_e = 2.1$ L mol^{-1} (Fig. 2, *a*), and processing by Eq. (7) for the region with $n < 2$ (route R-1) minus the contribution of route R-2 of the same system gives the first-order rate constant $k_1 = 0.1$ s^{-1} and $K_e = 2.39$ L mol^{-1} (Fig. 2, *b*). The coincidence of the values of the formation constant K_e of H-complex **2c** for the regions with $n < 2$ and $n = 2$ for the same system and its correspondence to the values of formation constants of similar H-complexes obtained in other studies[12] testify to the validity of the chosen reaction mechanism *via* routes R-1 and R-2. The experimental data for other systems (Table 2) were processed by Eqs. (7) and (8). In these cases, the satisfactory coincidence of the K_e values of routes R-1 and R-2 is also observed.

The analysis of the data in Table 2 shows that the formation constants K_e of complexes **2a—c** for **1a—c** are

Scheme 4



close, and the absolute values of the rate constants k_2 for the reaction with piperidine for compounds **1a—c** are also close. The same is valid for reactions with morpholine, and the reactivity of morpholine, as should be expected, is lower than that of piperidine. Of note is the high difference in k_2 values for **1b** and **1d** (~30-fold), *i.e.*, when the N—O˙ group in the cycle is substituted for N—Me. The reasons for this difference will be considered in detail elsewhere.

The experimental data were also processed on the assumption that the reactions of **1a—c** with amines can involve the dimeric form of amine (Scheme 5). In the concentration range from 0.1 to 0.4 mol L^{-1}, the reaction order with respect to the dimeric form of amine is equal to 1. The kinetic and thermodynamic parameters of the reactions of **1a—c** with amines in the assumption of routes R-1 and R-3 are listed in Table 2, and Fig. 3 illustrates the dependence of $1/k_{exp}$ on $1/[\mathbf{B}_D]$ for the

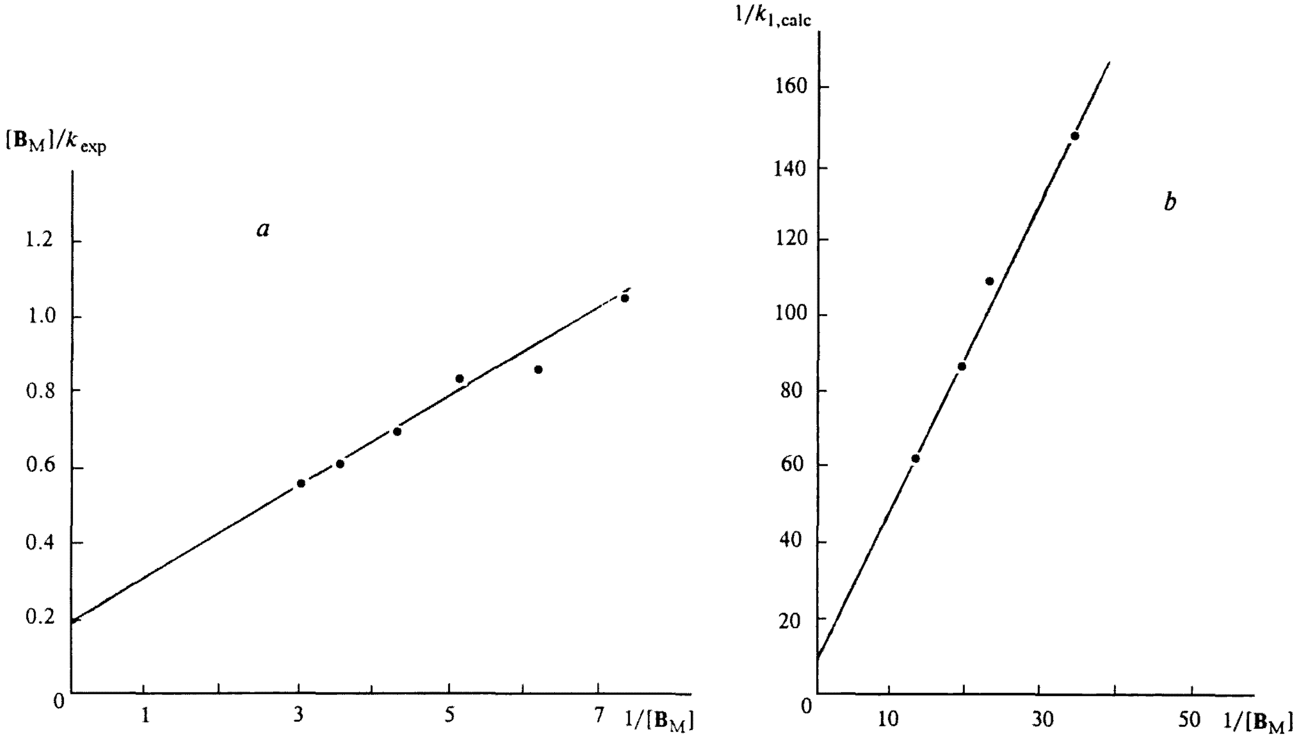
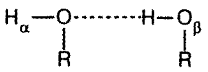


Fig. 2. *a.* Dependence of $[\mathbf{B}_\mathrm{M}]/k_\mathrm{exp}$ on $1/[\mathbf{B}_\mathrm{M}]$ for the **1c**—piperidine system with the reaction order with respect to piperidine $n = 2$. *b.* Dependence of $1/k_\mathrm{1,calc}$ on $1/[\mathbf{B}_\mathrm{M}]$ for the same system in the region with the reaction order with respect to piperidine $n = 1$.

1c—piperidine system. As can be seen from Table 2, the rate constants k_3 for the reaction involving the dimeric form of amine considerably exceed the rate constants k_1 for the reaction involving the monomeric form in each system, despite more favorable steric conditions for the latter. Probably, the proton-donating ability and nucleophilicity of the dimeric form of amine and dimers of alcohols and phenols are analogous.



$$H_\alpha-\underset{R}{O}\cdots\cdots H-\underset{R}{O_\beta}$$

The quantum-chemical calculations show a decrease in the electron density on the H_α atom and an increase in the electron density on the O_β atom compared to the corresponding monomeric forms of alcohols and phenols.[13,14] Thus, one can expect on going to dimeric

Table 2. Kinetic and thermodynamic parameters of reactions of compounds **1a**—**d** with piperidine and morpholine in hexane at 22 °C

Route	Amine	Constant	Values of constants for			
			1a	**1b**	**1c**	**1d**
R-1+R-2	Piperidine	k_2/L mol^{-1} s^{-1}	1.23	5.88	4.4	0.18
		K_e/L mol^{-1}	2.5	2.96	2.08	1.75
		k_1/s^{-1}	0.021	0.078	0.1	—
		K_e/L mol^{-1}	3.88	5.7	2.39	—
	Morpholine	k_2/L mol^{-1} s^{-1}	0.23	1.3	0.96	—
		K_e/L mol^{-1}	2.65	2.91	2.9	—
R-1+R-3	Piperidine	k_3/s^{-1}	0.42	3.16	1.59	0.091
		K_e'/L mol^{-1}	20.3	13.9	16.4	9.74
		k_1/s^{-1}	0.034	0.21	0.12	—
		K_e/L mol^{-1}	2.7	2.34	2.3	—
	Morpholine	k_3/s^{-1}	0.03	0.171	—	—
		K_e'/L mol^{-1}	7.9	8.21	—	—

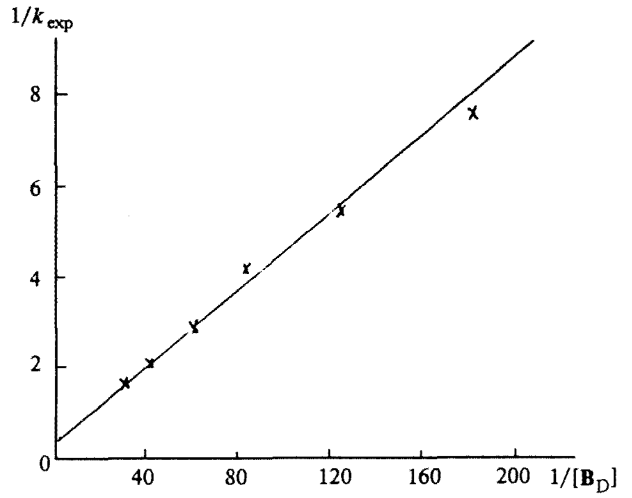


Fig. 3. Dependence of $1/k_{exp}$ on $1/[\mathbf{B}_D]$ for the reaction of **1c** with piperidine.

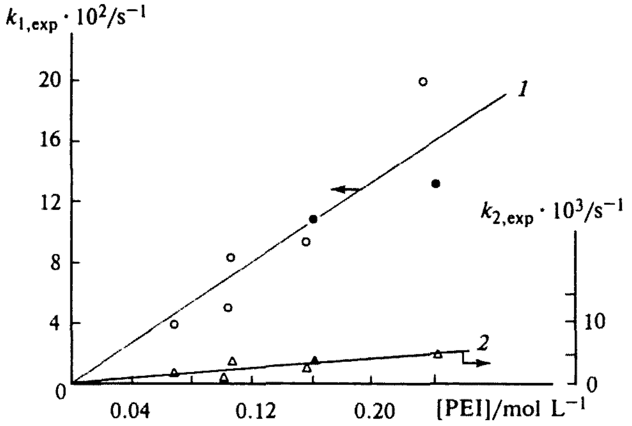
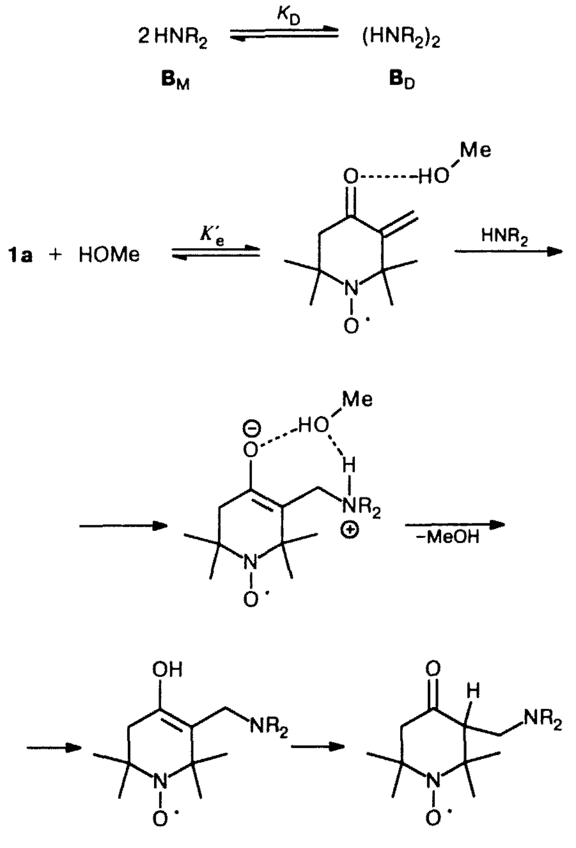


Fig. 4. Dependence of rate constants k_{exp} of mono- (*1*) and bis-addition (*2*) of PEI to **1b** in methanol on the concentration of PEI.

forms of amines an easier addition of the H atom of the dimer to the O atom of the keto group and enhancement of the efficiency of the nucleophilic attack compared to the monomeric form of amine. High values of the formation constants K_e' of H bonds involving the dimeric form of the amine are also observed for derivatives of salicylic acid and amines.[15]

Scheme 5



Compounds **1a—c** are of practical interest for the introduction of a spin probe into polymers containing NH groups. The kinetics of the reactions of **1a—c** with macromolecules containing NH groups can possess several specific features. Linear polyethyleneimine (PEI) was used in this work to elucidate this question. This polymer is also of interest, because its nitroxyl modification can be used for the study of its structural peculiarities and, in addition, it can be considered as one of the ways for preparation of a more efficient stabilizing agent based on PEI.[16] The kinetic studies were performed using as an example the **1b**—PEI system in methanol (because of the poor solubility of the polymer in hexane).

One of the peculiarities of the reaction in methanol is the specific interaction of MeOH to form the H bond of alcohol with the O atom of the keto group of **1b** instead of amine and the formation of the H bond of the alcohol with the NH groups of PEI. It turned out that the reaction order with respect to PEI is equal to 1. This can be explained in terms of Scheme 4 by the participation of associates of the initial components with methanol and probably, as a consequence, by the participation of the alcohol in the proton transfer to form the system of hydrogen bonds in the bipolar ion of the **C′** type (see Scheme 4). The rate constants for the reaction of **1b** with PEI were calculated on the assumption that this is the two-stage process, as in the case of the **1b**—piperidine system, with consecutive involvement of the methylene groups of **1b**. Constants k_{exp} of the both stages are presented in Fig. 4, and the second stage is considerably slower than the first one.

The two-stage character of the process could be associated, for example, with the difference in the reactivities of particular NH groups of PEI. However, under the

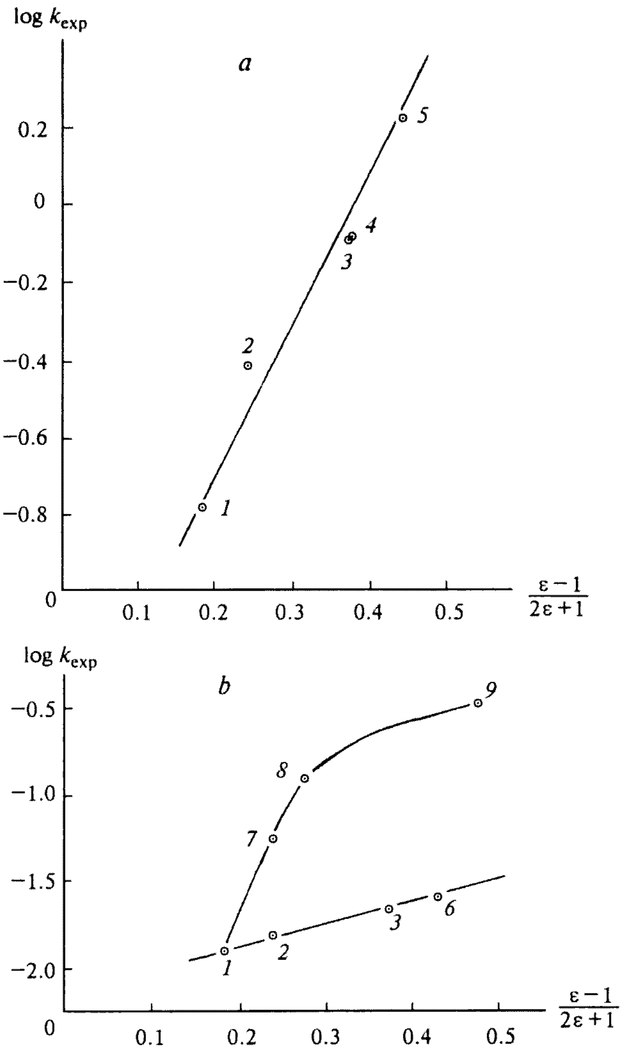
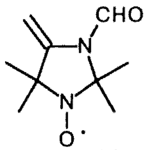


Fig. 5. *a*. Dependence of constants k_{exp} of the reaction of **1b** (*a*) and **1d** (*b*) with piperidine on the dielectric constant of the medium. *1*, hexane; *2*, toluene; *3*, chlorobenzene; *4*, hexane—acetone (40 : 6); *5*, hexane—acetone (1 : 1), *6*, *o*-dichlorobenzene; *7*, hexane—methanol (99.5 : 0.5); *8*, hexane—methanol (99 : 1); *9*, methanol.

conditions used for **1b**, compounds **1c** and 

, with one reactive methylene group, are consumed in the reaction with PEI (C_0 = 0.225 mol L^{-1}) in one stage with the reduced constants ($k_1' = k_{\text{exp}}/[\mathrm{B}_0]$) k_1' = 3.8 · 10^{-4} L mol^{-1} s^{-1} and k'_1 = 1.74 · 10^{-3} L mol^{-1} s^{-1}, respectively, calculated per PEI unit. Therefore, the two-stage character of the reaction of **1b** with PEI can be explained in the following way. After addition of PEI to one of two methylene groups of **1b** (first stage of the reaction), two routes are possible for the reaction of the second methylene group of **1b**: with the NH group of another PEI molecule or with the NH group of the same molecule. In the first case, two polymeric chains of PEI are cross-linked, and in the second case, an intramolecular cyclization takes place. Since k_{exp} of both stages depend on the concentration of PEI (see Fig. 4), the cross-linkage of two polymeric chains is realized. For both stages of the reaction, the reduced rate constants calculated per NH group are the following: k_1' = 5.8 · 10^{-3} and k_2' = 1.8 · 10^{-4} L mol^{-1} s^{-1}. The reaction of **1b** with diethylamine in methanol gives k_1' = 3.2 · 10^{-3} and k_2' = 4.3 · 10^{-4} L mol^{-1} s^{-1}, respectively.

The closeness of kinetic parameters for different reactions in methanol confirms that the assumptions concerning peculiarities of the reaction of **1b** with PEI in methanol are valid.

The effect of the medium on the addition reaction was considered in more detail using as an example reactions of **1b** and **1d** with piperidine in *n*-hexane, toluene, chlorobenzene, *o*-dichlorobenzene, acetone—hexane mixtures, methanol, and its mixtures with hexane. These reactions can be considered as the interaction of two polar molecules. The corresponding rate constants should depend on the change in dielectric permeability of the medium and obey the Kirkwood equation.[17] In both cases, a linear dependence of log$k$ on $(\varepsilon-1)/(2\varepsilon+1)$ holds for methanol-free systems. For the **1b**—piperidine system (C_0 = 0.125 mol L^{-1}), this dependence is well fulfilled: $\log k_{\text{exp}} = -1.35 + 3.43(\varepsilon-1)/(2\varepsilon+1)$ (10) (Fig. 5, *a*), and for the **1d**—piperidine system (C_0 = 0.25 mol L^{-1}) in aprotic solvents, $\log k_{\text{exp}} = -2.13 + 1.3(\varepsilon-1)/(2\varepsilon+1)$ (11) (Fig. 5, *b*).

When methanol or its mixtures with hexane are used as solvents, an overestimated value of k_{exp} is observed. For example, for the **1d**—piperidine system (see Fig. 5, *b*) with account of Eq. (11), the k_{exp} value for this reaction in methanol should be 0.03 s^{-1}. In fact, k_{exp} = 0.3 s^{-1}. In this case, the specific participation of methanol in the formation of H bonds and, probably, in the proton transfer during the formation of H bonds in the bipolar ion of the **C′** type (one of the variants of Scheme 5) should be taken into account along with the Coulomb interaction between the reacting particles. This can explain why the reaction is first order with respect to the amine.

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References

1. A. D. Malievskii, F. B. Shapiro, I. V. Yakovleva, and S. I. Koroteev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, 642 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37**, 542 (Engl. Transl.)].
2. A. B. Lutskii and E. I. Goncharova, *Zh. Fiz. Khim.*, 1966, **40**, 2735 [*Russ. J. Phys. Chem.*, 1966, **40** (Engl. Transl.)].
3. R. V. Golovnya, I. P. Zhuravleva, S. V. Zenin, V. A. Polyakov, and G. B. Sergeev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1973, 2595 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1973, **22** (Engl. Transl.)].

4. A. M. Belostotskii and A. B. Shapiro, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 486 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 421 (Engl. Transl.)].
5. A. B. Shapiro and V. I. Suskina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1985, 414 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1985, **34**, 378 (Engl. Transl.)].
6. G. C. Pimentel and A. L. McClellan, *The Hydrogen Bond*, Ed. L. Pauling, San Francisco—London, 1960.
7. N. Z. Yalysheva, N. P. Solov'eva, V. V. Chistyakov, Yu. N. Sheinker, and V. G. Granik, *Khim. Geterotsikl. Soedin.*, 1986, 1118 [*Chem. Heterocycl. Compd.*, 1986 (Engl. Transl.)].
8. H. E. Affsprung, S. D. Chriistian, and J. D. Worley, *Spectrochim. Acta*, 1964, **20**, 1415.
9. A. A. Petrov, *Khimiya alkenov* [*Chemistry of Alkenes*], Khimiya, Leningrad, 1969 (in Russian).
10. L. I. Kostenko, A. F. Popov, V. V. Kravchenko, and I. F. Perepichka, *Zh. Obshch. Khim.*, 1986, **22**, 245 [*J. Gen. Chem. USSR*, 1986, **22** (Engl. Transl.)].
11. *Vodorodnaya svyaz'* [*Hydrogen Bond*], Ed. N. D. Sokolov, Nauka, Moscow, 1981 (in Russian).
12. L. V. Vladimirov, S. A. Artemenko, V. V. Ivanov, A. N. Zelenetskii, E. F. Oleinik, and O. B. Salamatina, *Vysokomol. Soedin.*, 1980, **22A**, 225 [*Polym. Sci. USSR*, 1980, **22A** (Engl. Transl.)].
13. R. P. Tiger, E. Yu. Bekhli, S. P. Bondarenko, and S. G. Entelis, *Zh. Obshch. Khim.*, 1973, **9**, 1563 [*J. Gen. Chem. USSR*, 1973, **9** (Engl. Transl.)].
14. V. P. Volkov, E. S. Naidovskii, B. A. Komarov, A. I. Kuzaev, and B. A. Rozenberg, *Vysokomol. Soedin.*, 1982, **24A**, 2520 [*Polym. Sci. USSR*, 1982, **24A** (Engl. Transl.)].
15. S. F. Bureiko and V. P. Oktyabr'skii, *Zh. Fiz. Khim.*, 1985, **4**, 1403 [*Russ. J. Phys. Chem.*, 1985, **4** (Engl. Transl.)].
16. P. A. Gembitskii, D. S. Zhuk, and V. A. Kargin, *Polietilenimin* [*Polyethyleneimine*], Nauka, Moscow, 1971 (in Russian).
17. S. G. Entelis and R. P. Tiger, *Kinetika reaktsii v zhidkoi faze* [*Kinetics of Liquid-Phase Reactions*], Khimiya, Moscow, 1973 (in Russian).

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