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Antiradical Activity of Aryl- and Hetarylhydrazones in Ethylbenzene Oxidation

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Abstract—A relation between the kinetic parameters of the antiradical activity of aryl and hetarylhydrazones and their electronic structure is revealed in the form of the correlation between the reaction rate constants, bond energies of the reaction centers and the antioxidants ionization potentials. The relations obtained can be used to predict the antiradical activity in a series of hydrazones.

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A variety of organic substances, materials, and composition suffer oxidative aging under the influence of the air oxygen. To retard the radical–chain oxidation processes antioxidants are used. Planning and synthesis of new antioxidants is commonly carried out empirically, and success in the selection and creation of new oxidation inhibitors today is a result of practice rather than the consistent application of the theory.

In previous studies we have found that arylhydrazones of aromatic aldehydes are effective inhibitors of the oxidation of organic compounds [1, 2]. We have shown that the antioxidant action of these compounds is due to the oxidation chain termination in the reaction with the peroxide radicals of the oxidized substrate. The reaction rate constants of arylhydrazones with the peroxide radicals of ethylbenzene were measured. The extension of the array of antioxidants of hydrazone series and the measurement of the kinetic parameters of their reactions can provide the data relating the reactivity of various hydrazones in the reactions of inhibited oxidation with their structure and to reveal the correlation between the parameters of the antiradical activity of hydrazones and characteristics of their electronic structure. Such correlations may permit the assessment of the reactivity of other hydrazones in the reaction with peroxy radicals without carrying out experiments, and to plan the synthesis of more effective antioxidants.

The goal of this work was a study of the inhibitory action of the hetarylhydrazones of aromatic aldehydes in the initiated oxidation of ethylbenzene and revealing the components of the molecular structure of aryl- and hetarylhydrazones responsible for their reactivity in the reaction with peroxide radicals.

Kinetics of the processes was studied using a chemiluminescence method. As an activator of luminescence in the chemiluminescent studies dibromoanthracene was used, initiator of oxidation was azodiisobutyronitrile. The antiradical activity of the inhibitors (InH) was characterized by the rate constant (k_7) in the reaction of a studied compound with the peroxyradicals $RO_2^{\cdot}$ formed at the oxidation of the substrate.

For the synthesis of aryl- and hetarylhydrazones we used the condensation reactions of appropriate hydrazine derivatives with benzaldehyde in alcohol solution. The identity and purity of synthesized hydrazones was established by UV, IR, and ^{1}H NMR spectroscopy and by thin layer chromatography.

A glow arising in the process of liquid-phase oxidation of organic compounds is due to the recombination of peroxy radicals in the reaction [3]:

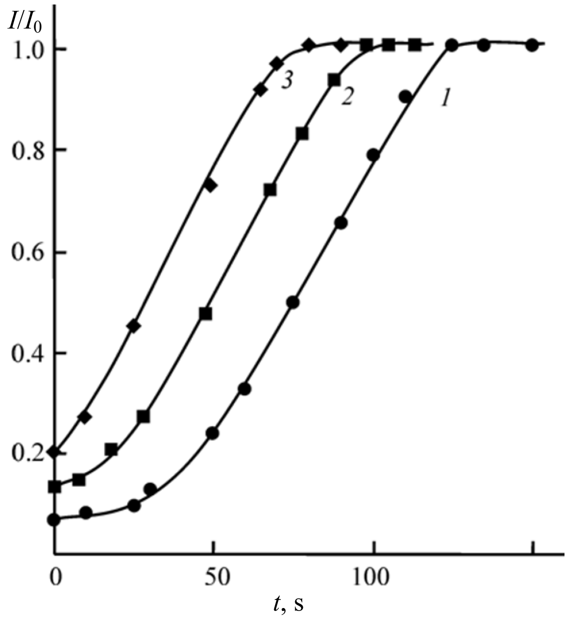


Fig. 1. Kinetic curves of changes in the relative intensity of chemiluminescence at the initiated oxidation of ethylbenzene in the presence of 2-benzylidene-1-(pyridine-3-yl) hydrazine (inhibitor no. 8 in Table 1). $[\mathrm{InH}]_0$, M: (*1*) 2×10^{-5}, (*2*) 1×10^{-5}, (*3*) 5×10^{-6}, $W_\mathrm{i} = 5.4\times10^{-7}$ mol l^{-1} s^{-1}, $T = 343$ K.

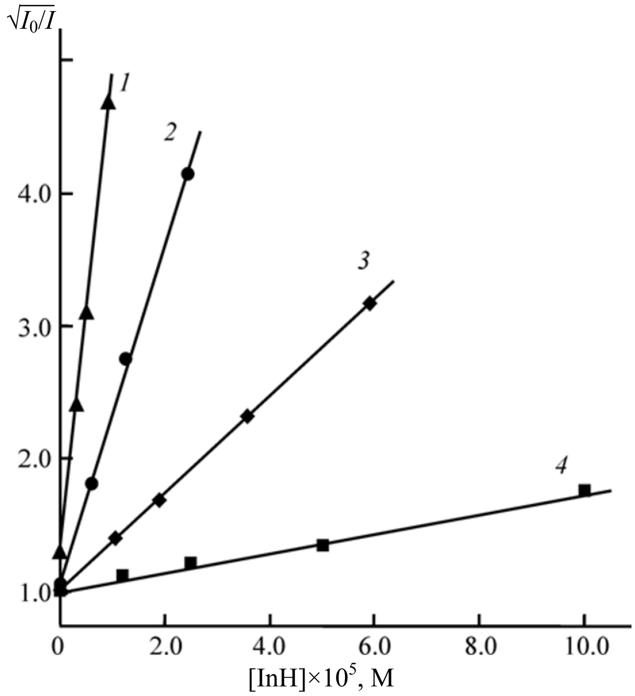


Fig. 2. Relative intensity (I_0/I) of chemiluminescence at the oxidation of ethylbenzene vs. inhibitor concentration: (*1*) inhibitor no. 1, (*2*) inhibitor no. 9, (*3*) inhibitor no. 6, (*4*) inhibitor no. 3 (see Table 1). $W_\mathrm{i} = 5.4\times10^{-7}$ mol l^{-1} s^{-1}, $T = 343$ K.

$$\mathrm{RO}_2^{\bullet} + \mathrm{RO}_2^{\bullet} \xrightarrow{k_6} [\mathrm{ROOOOR}] \rightarrow \mathrm{R{=}O}^* \rightarrow \mathrm{R{=}O} + h\nu.$$

It was found experimentally that adding the studied hydrazone derivatives to ethylbenzene leads to a decrease in the chemiluminescent emission at its oxidation. Consequently, the hetarylhydrazones react with peroxy radicals of the substrate at the oxidation of the latter according to Eq. (1), as confirm the chemiluminesce dependencies shown in Fig. 1.

$$\mathrm{RO}_2^{\bullet} + \mathrm{InH} \xrightarrow{k_7} \mathrm{ROOH} + \mathrm{In}^{\bullet}. \quad (1)$$

Using Eq. (2) and the dependences shown in Fig. 2, we calculated rate constants of the reactions of hetarylhydrazones with peroxy radicals [3]. Table 1 lists the results of the calculations.

$$\sqrt{I_0/I} = 1 + 1.1(k_7/\sqrt{k_6 W_i})[\mathrm{InH}]. \quad (2)$$

As follows from the results, the difference in the rate constant in the studied series of compounds is about three orders of magnitude, namely, there is a significant dependence of the constants on the molecular structure.

To quantify the influence of the structure of aryl- and hetarylhydrazones on their antiradical activity in the reaction (1), we carried out quantum-chemical calculations of the characteristics of the electronic structure of molecules and the corresponding radicals formed in the reaction (1), as well as the structure of the corresponding transition states of this reaction.

The quantum-chemical calculations were carried out in AM1 approximation using the MOPAC2009 software package [4]. For all the calculated structures the geometry optimization over all independent variables was carried out and the additional proof of the localization of the energy minima was performed by the calculation of the vibration spectra. The open-shell systems were calculated in the approximation of the unlimited Hartree–Fock method.

The identification of transition states was carried out by the presence of one imaginary frequency in the vibration spectrum and further tested by the evolution of the system along the internal reaction coordinate from the transition state down along the reaction channels in the directions of both the reactants and the reaction products. Energies of N–H and O–H bonds ($D_{\mathrm{X–H}}$) were calculated by Eq. (3):

$$D_{\mathrm{X–H}} = \Delta H_{\mathrm{In}^{\bullet}} + 218.13 - \Delta H_{\mathrm{InH}}, \quad (3)$$

Table 1. Antiradical activity (k_7), calculated energy of N–H and O–H bonds ($D_{\mathrm{N–H}}$, $D_{\mathrm{O–H}}$), and ionization potentials (J_{InH}) of aryl- and hetarylhydrazone molecules

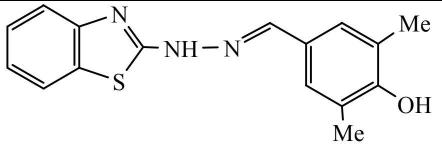
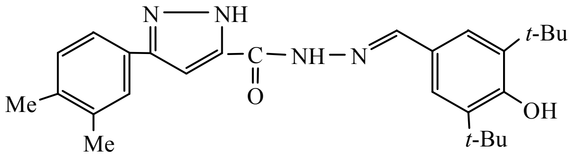
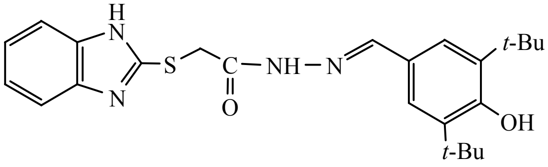
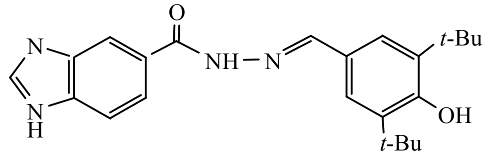
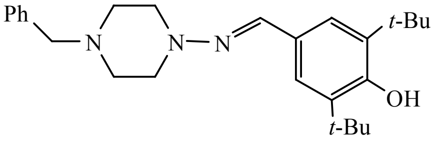
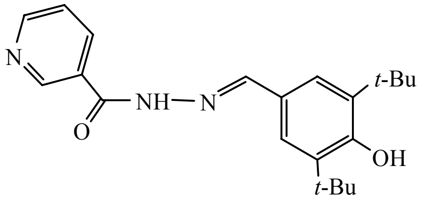
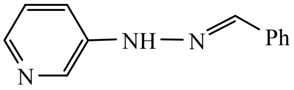
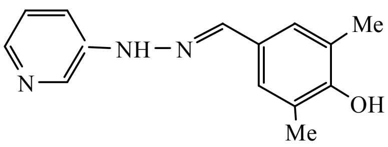
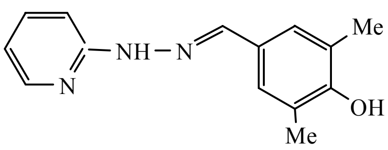
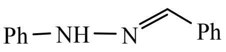
Run no.	Inhibitor	k_7, l mol^{-1} s^{-1}	$D_{\mathrm{N–H}}$, kJ mol^{-1}	$D_{\mathrm{O–H}}$, kcal mol^{-1}	J_{InH}, eV
1		$(9.3\pm0.4)\times10^5$	270.8	308.5	8.45
2		$(3.9\pm0.4)\times10^4$	296.3	311.5	8.72
3		$(2.0\pm0.1)\times10^4$	297.6	313.4	8.55
4		$(2.6\pm0.3)\times10^4$	297.3	–	8.37
5		$(4.2\pm0.2)\times10^4$	–	294.8	8.23
6		$(1.00\pm0.05)\times10^5$	299.4	301.1	8.54
7		$(6.6\pm0.3)\times10^5$	265.6	–	8.55
8		$(5.2\pm0.3)\times10^5$	261.9	307.0	8.37
9		$(3.5\pm0.2)\times10^5$	283.4	308.7	8.31
10		$(1.20\pm0.07)\times10^6$	262.8	–	8.15

Table 1. (Contd.)

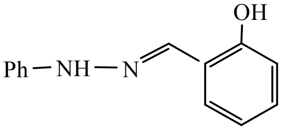
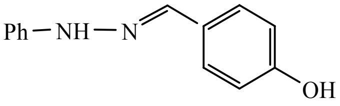
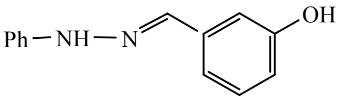
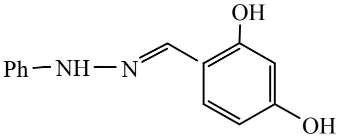
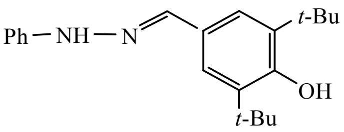
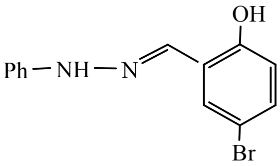
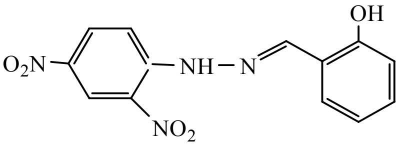
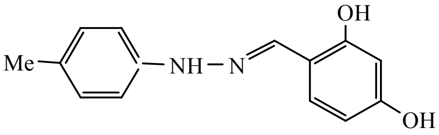
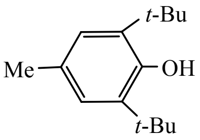
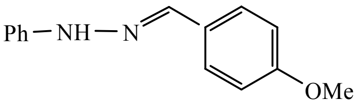
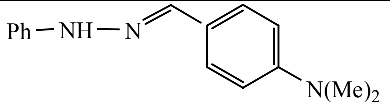
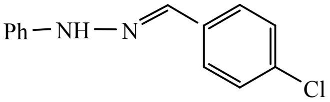
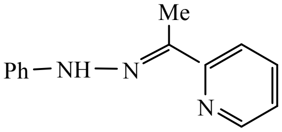
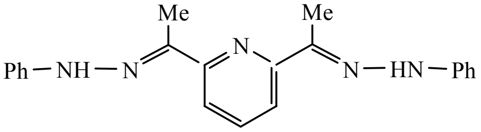
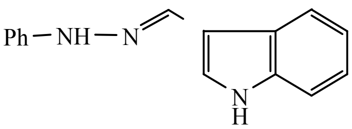
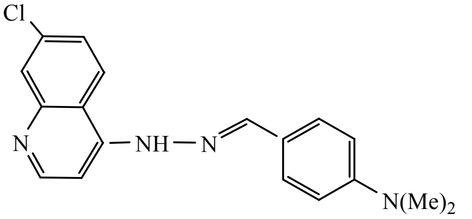
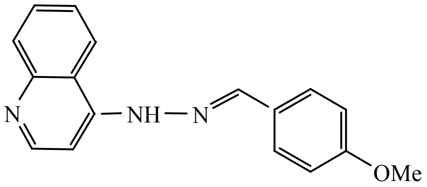
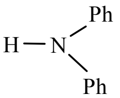
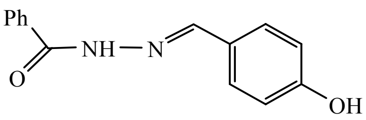
Run no.	Inhibitor	k_7, l mol^{-1} s^{-1}	$D_{N–H}$, kJ mol^{-1}	$D_{O–H}$, kcal mol^{-1}	J_{InH}, eV
11		$(1.3\pm0.1)\times10^6$	261.5	305.2	8.02
12		$(1.35\pm0.30)\times10^6$	263.8	314.3	8.29
13		$(1.07\pm0.25)\times10^6$	264.7	323.1	8.41
14		$(2.7\pm0.2)\times10^6$	263.5	306.1 (*o*) 312.5 (*p*)	8.19
15		$(2.6\pm0.3)\times10^6$	261.3	307.4	8.2
16		$(7.7\pm0.4)\times10^5$	264.2	319.4	8.4
17		$(1.26\pm0.09)\times10^4$	305.1	319.4	9.12
18		$(3.0\pm0.2)\times10^6$	261.5	305.1 (*o*) 311.1 (*p*)	8.13
19		$(3.1\pm0.2)\times10^4$	–	294.8	8.62
20	Ph–OH	$(3.00\pm0.07)\times10^3$	–	331.1	9.11
21		$(1.24\pm0.09)\times10^6$ [1]	263.3	–	8.23

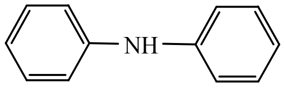
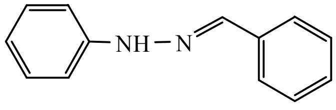
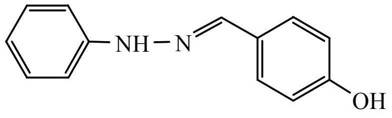
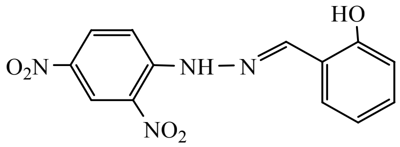
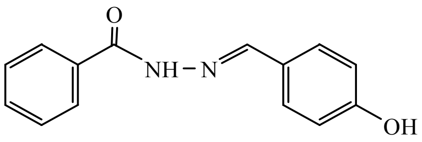
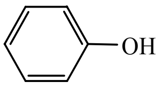
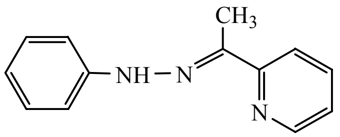
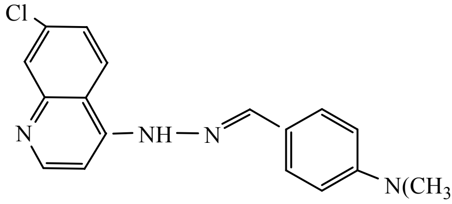
Table 1. (Contd.)

Run no.	Inhibitor	k_7, l mol^{-1} s^{-1}	$D_{N–H}$, kJ mol^{-1}	$D_{O–H}$, kcal mol^{-1}	J_{InH}, eV
22		$(1.3±0.2)×10^6$	262.0	–	7.95
23		$(1.18±0.09)×10^6$	264.5	–	8.45
24		$(3.20±0.1)×10^5$	273.3	–	8.49
25		$(5.1±0.2)×10^5$	278.7	–	8.50
26		$(3.5±0.4)×10^6$	254.8	–	7.96
27		$(1.33±0.05)×10^6$	258.2	–	8.20
28		$(2.8±0.4)×10^5$	254.4	–	8.48
29		$(1.1±0.1)×10^6$	253.3	–	8.28
30		$(5.0±0.2)×10^4$	305.1	–	8.12
31		$(2.4±0.1)×10^3$	302.9	318.4	8.61

where ΔH_{In}• is the standard enthalpy of formation of the radical from the inhibitor, ΔH_{InH} is the standard enthalpy of formation of the molecule. The values obtained are listed in Table 1.

Naturally, the reactivity of the molecules of aryl- and hetarylhydrazones in reaction (1) is determined by the properties of the transition state. To simplify the calculations, the interaction of compounds of the

Table 2. Electronic, structural and energy characteristics of the transition state of model reactions of aryl- and hetarylhydrazones with the peroxy radical

Reactant	Reaction coordinate	$\Delta H^{\#}$	$\nu^{\#}\cdot i$	$R^{\#}_{\mathrm{X-H}}$	$R^{\#}_{\mathrm{H-O}}$	$q^{\#}_{\mathrm{X}}$	$q^{\#}_{\mathrm{H}}$	$q^{\#}_{\mathrm{O}}$
	←N···H→←O	135.4	–5723	1.217	1.331	–0.126	0.226	–0.276
	←N···H→←O	114.0	–5743	1.210	1.354	–0.100	0.205	–0.276
	←N···H→←O	112.7	–5797	1.208	1.356	–0.099	0.205	–0.275
″	←O···H→←O	138.5	–3846	1.174	1.208	–0.271	0.230	–0.211
	←N···H→←O	137.5	–5079	1.287	1.279	–0.128	0.219	–0.215
″	←O···H→←O	139.5	–3835	1.182	1.206	–0.274	0.232	–0.205
	←N···H→←O	145.7	–5288	1.253	1.296	–0.193	0.211	–0.245
″	←O···H→←O	146.5	–3791	1.177	1.204	–0.271	0.230	–0.208
	←O···H→←O	148.7	–3766	1.187	1.193	–0.269	0.229	–0.205
	←N···H→←O	123.9	–5658	1.220	1.345	–0.103	0.211	–0.271
	←N···H→←O	113.1	–5422	1.221	1.339	–0.131	0.216	–0.224

[a] $\Delta H^{\#}$ is activation enthalpy (kJ mol^{-1}), $\nu^{\#}\times i$ is the imaginary vibration frequency (cm^{-1}), $R^{\#}$ is interatomic distance (Å) between atoms of the reaction sites in the transition state, $q^{\#}$ is electric charges on the atoms of the reaction sites.

hydrazone series with the peroxyradicals of the oxidized substrate was simulated as a hypothetical reaction with the simplest peroxide radical $HO_2^{\bullet}$:

$$HO_2^{\bullet} + InH \rightarrow HOOH + In^{\bullet}$$

Table 2 lists the results of calculation of the characteristics of transition states in the model reactions of individual aryl- and hetarylhydrazones. For this series were selected, the molecules with the reactivity varying in the range of three orders of magnitude. The activation barrier of the reaction corresponding to the activation enthalpy ($\Delta H^{\#}$) was calculated by Eq. (4):

$$\Delta H^{\#} = \Delta H_{\mathrm{TS}} - \Delta H_{\mathrm{InH}} - \Delta H_{\mathrm{HO_2^{\bullet}}}, \quad (4)$$

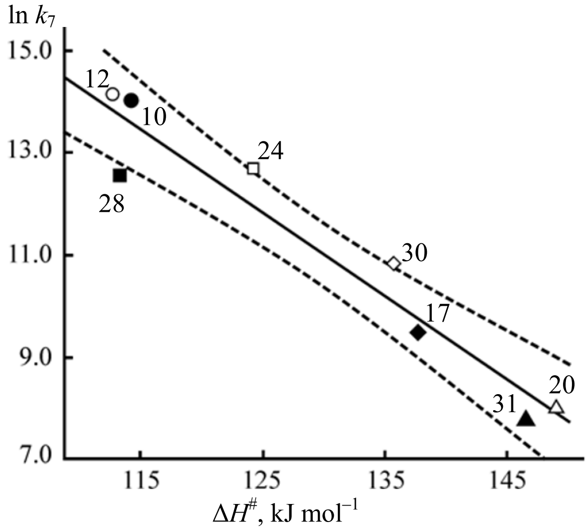


Fig. 3. Correlation between the logarithm of experimental rate constants (k_7) and the calculated value of the enthalpy of activation of $\Delta H^{\#}$ (for the numbering, see Table 1).

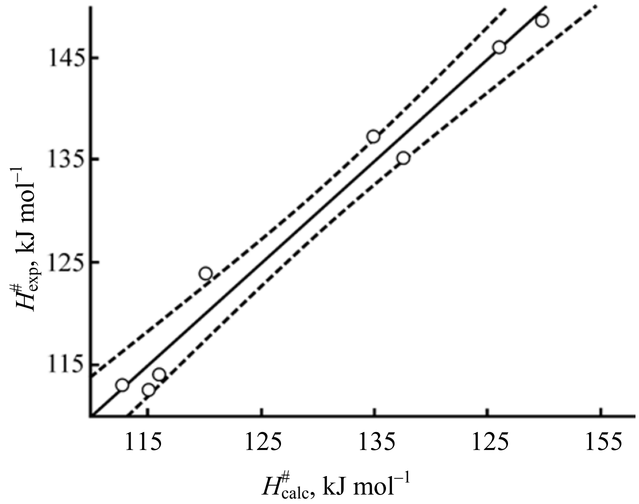


Fig. 4. The dependence of the enthalpy of activation $\Delta H^{\#}$ on the strength of the X–H bond ($D_{\text{X–H}}$) and ionization potential of aryl- or hetarylhydrazones J_{InH}.

where ΔH_{InH} is the standard enthalpy of formation of the inhibitor molecule, $\Delta H_{\text{HO2·}}$ is the standard enthalpy of formation of hydroperoxide radical, ΔH_{TS} is the standard enthalpy of formation of the transition state.

Some of these molecules have in their structure not only NH, but also OH groups. Therefore, we also investigated the competing reaction of the hydrogen atom abstraction from the O–H bond by the $HO_2^{\bullet}$. As follows from the results obtained (Table 2), the imaginary frequencies corresponding to modes of the reaction coordinates are antisymmetric vibrations of the type ←X···H→←O (where X is nitrogen or oxygen). In the case of the splitting off the hydrogen atom from the N–H bond the activation barrier is characterized by steeper slope compared with the attack on the O–H group ($\nu^{\#}_{\text{N–H}} > \nu^{\#}_{\text{O–H}}$).

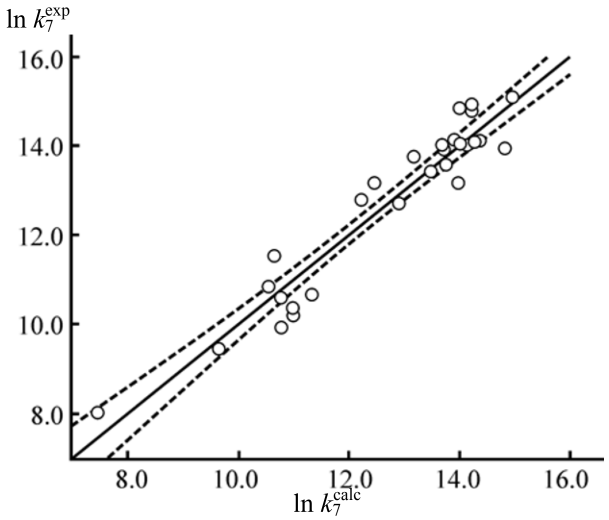


Fig. 5. Comparison of the logarithms of rate constants: experimental and calculated by Eq. (3).

When the molecule contains the reactive bonds of both types, the activation barrier for reactions involving the N–H bonds is less. Figure 3 shows a good linear relationship between the logarithm of the rate constants and the calculated value of activation enthalpy $\Delta H^{\#}$, that is, in the molecules containing both N–H and O–H bonds the cleavage of the former is preferable.

In the investigated series of reactions in the saddle points the X–H bond of the reaction site is stretched by 20–25% compared to that in the isolated molecule, that is, the transition state of this series of reactions can be regarded as the so-called *early transition state*. In this case, the properties of the transition state should largely be determined by the characteristics of the reactants. It was shown in [5–8] that peroxy radicals can split off hydrogen atom of the molecules of various aromatic compounds from either alkyl, or hydroxy groups. The reactivity of the oxidized molecule is determined therefore by the strength of the C–H and the O–H bonds ($D_{\text{X–H}}$), as well as by their electron-donor properties, i.e., by their ionization potentials (J_{InH}). As show the data in Table 2, the transition state of hydrazones is polar with a partial charge transfer from the atoms of the molecule to the atoms of the peroxy radical. Figure 4 shows the dependence of $\Delta H^{\#}$ on $D_{X–H}$ and J_{InH}. The equation of this relation is as follows, with the correlation coefficient 0.988:

$$\Delta H^{\#} = -3.008 + 0.125D_{X–H} + 0.308J_{InH^{\bullet}}. \quad (5)$$

Since for the investigated series of molecules the reaction sites in the transition state of the reaction are of the same type, we can assume that the studied series is isoentropic one, which is confirmed by the above relationship plotted in Fig. 3.

Based on the above arguments we obtained the correlation that describes the entire series of the studied reactions, which can be represented by Eq. (6) and the plot in Fig. 5, with the correlation coefficient 0.966.

$$\ln k_7 = 43.681 - 0.085D_{X–H} - 0.903J_{InH}, \quad (6)$$

where $\ln k_7$ is the logarithm of the calculated (predicted) rate constants for reaction (1).

Analysis of the dependence of the rate constants in the reaction of $RO_2^{\bullet}$ with the molecules of compounds of the hydrazone series on the parameters of the electronic structure allows a conclusion that the high reactivity of hydrazones is determined, on the one hand, by the energy factor (energy of the cleaving bonds), and on the other hand, by the polarity, which is manifested in the ability of the species to release electrons in the transition state. In general analyzing the results we note that the value of the N–H bond strength in the compounds of hydrazone series is considerably lower than in the typical amine antioxidant, diphenylamine. This explains the higher reactivity of aryl- and hetarylhydrazones compared to aromatic amines in the reaction with the peroxy radicals formed from ethylbenzene. In going from the arylhydrazones to nitrogen-containing hetarylhydrazones the $D_{N–H}$ increases, while the antiradical activity is naturally reduced. A comparison of $D_{N–H}$ and $D_{O–H}$ in aryl- and hetarylhydrazones of hydroxybenzaldehydes indicates that the N–H bond is less strong, and hence is more reactive toward peroxy radicals. Therefore, the NH group of the hydrazone fragment contributes to the antiradical activity of hydroxybenzaldehyde hydrazones.

The found correlations of antiradical activity of aryl- and hetarylhydrazones with the characteristics of their electronic structure allows a prediction of the reactivity of the compounds in the reactions with peroxy radicals. This is particularly important at planning the syntheses of new antioxidants of the hydrazone series. The forecast of the reactivity of the designed inhibitors allows the evaluation of the prospects of their practical application.

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