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ELECTRONIC STRUCTURE OF THE ORGANIC COMPOUNDS AND THEIR REACTIVITY IN THE REACTIONS OF RADICAL HYDROGEN ATOM TEAR BY HO$_2^\bullet$ RADICAL

Target. This paper presents the results of investigation the electronic structure of some organic molecules containing O-H and N-H bonds. The potential energy surfaces were obtained for the hydrogen abstraction by the peroxyl radical.

Technique. Self-consistent field (SCF) quantum-chemical calculations were performed at the Hartree-Fock level of theory in the approximation of the semiempirical method PM3.

Results. The points corresponding to the structures of the transition states were located on the potential energy surface and the activation parameters of the studied reactions were evaluated. The electronic and geometric characteristics of these reactions and the electronic and thermodynamic parameters of natural antioxidants, aromatic amines and phenols, were calculated.

Scientific novelty. The relation of the activation parameters of the reaction to the electronic characteristics of the starting materials was obtained. The antioxidant activity of a substance is determined by its electron-donor properties and the stability of the formed radical.

Practical value. These results allow predicting the antioxidant capacity of various naturally occurring inhibitors.

Key words: antioxidant effect, oxidation by peroxyl radical, phenolic compounds, heterocyclic molecules, Hartree-Fock method, the rate constant, activation energy, the electronic parameters.

Formulation of the problem. The highly-active free radicals are formed constantly in the living organism during the oxidation of lipids, proteins and nucleic acids creating conditions for the development of many different diseases. Substances that neutralize these reactive particles – antioxidants – are produced, to some extent, by the cell, but most of them are delivered with the food, especially of plant origin. The forecasting of the antioxidant activity of different substances depending on their structure is thus an extremely important goal.

Analysis of the latest research and publications showed that the oxidation inhibitors (InH), contained in the food, are related primarily to different types of phenolic compounds [1]. Primarily, these are flavonoids (formulas I-III), hydroxy acids and their derivatives (formula IV, V), polyphenols (formula VI, VII). Heterocyclic compounds containing nitrogen (mainly B vitamins, formula VIII, IX) and oxygen (E vitamins, the formula X) also have high antioxidant effect.

All these compounds possessing reducing properties and easily react with peroxyl radicals thus breaking the natural oxidation chain:
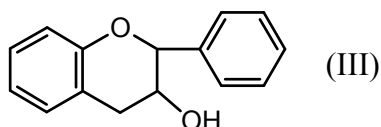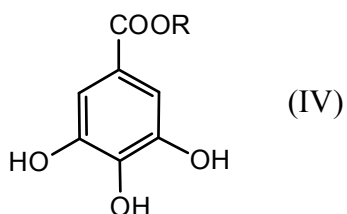
$$RO_2^\bullet + InH \xrightarrow{k_7} ROOH + In^\bullet. \qquad (1)$$
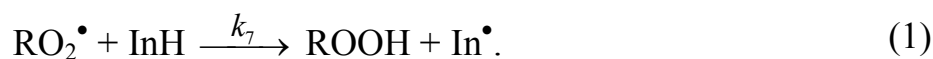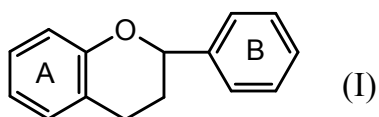
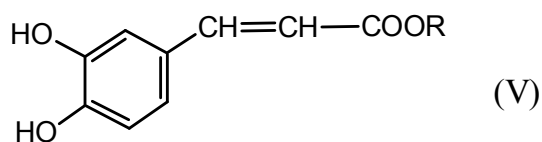I – a general formula of flavonoids, rings A and B may contain a different number of OH-groups

(I)
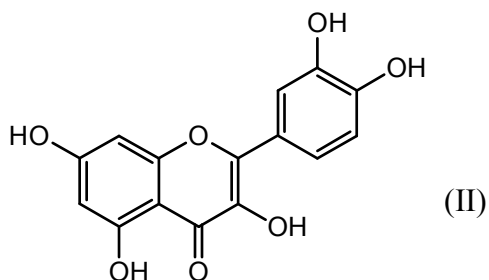
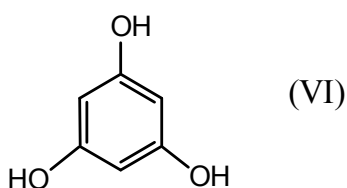(eg., II – quercetin – an antioxidant of tea, hops, onion, black currants, blackberries;

(II)

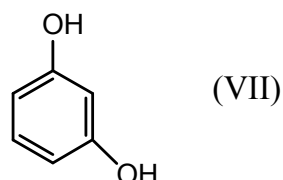III – catechin – antioxidant strawberry, peach);

(III)

IV – gallic acid derivatives (R – H, alkyl radical) are part of the plants of tea;

(IV)

V – caffeic acid derivatives (R – H, alkyl radical) are contained in the stone fruit;

(V)

VI – phloroglucinol – the component of the citrus fruits;

(VI)

VII – resorcinol – is a part of citrus fruit plants;

(VII)
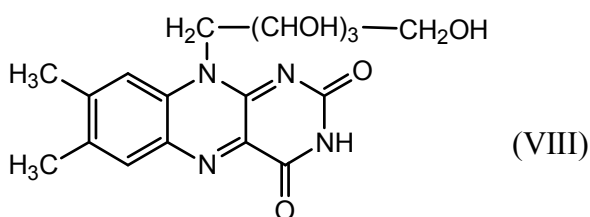
VIII – riboflavin (vitamin B_2) – is a part of the green leaf vegetables, legumes;

(VIII)
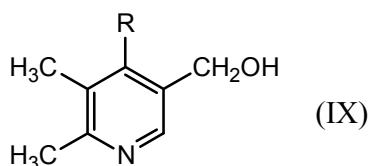
IX – the general formula of vitamins B_6 (R= –CHO, –CH$_2$NH$_2$, –CH$_2$OH) – components of green pepper, wheat, dry yeast;

(IX)

X – the total formula of tocopherols – derivatives of the tocol (R=R'=R"=H), which are found in vegetable oils.

(X)

The rate constant of the reaction (1) is a quantitative measure of the antioxidant activity of the inhibitor [2].

While the rate constant of hydrogen abstraction by peroxyl radicals can be calculated for the individual chemical compounds, most natural antioxidants present a complex mixture of substances, which is difficult to separate.

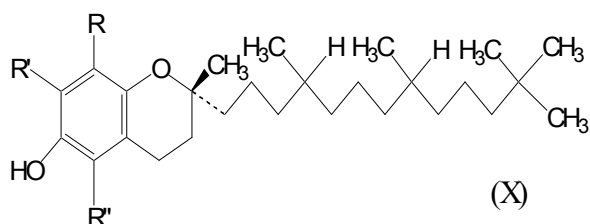A number of comprehensive studies of the kinetics of the reaction (1) have been conducted to date. The hydrocarbons of various structures and inhibitors, representing a variety of aromatic compounds with OH- and NH-groups analogous to natural antioxidants have been studied in this reaction.

The aim of this study was to investigate the effect of the features of the chemical structure of antioxidants on the reactivity of X-H bonds (where X is or N) towards oxidation.

Results and Discussion. The most complete information about the electronic structure of chemical compounds can be obtained by quantum-chemical methods. Here, we performed such studies using SCF approach within the restricted Hartree-Fock molecular orbitals theory, at PM3 approximation [3], as implemented in MOPAC 93 [4]. Geometry optimization was carried out in all degrees of freedom of the molecules (i.e., (3N-6) variables).

The optimization was performed until the the gradient $< 0,1$ kcal/(mol·Å) is reached and frequency calculations were used to confirm that the optimized structure in the minimum (by lack of imaginary frequencies).

In order to study the electronic nature of the transition state of the reaction (1), we have scanned the surface of the potential energy along the reaction coordinate for the reaction:

$$c\text{-}C_6H_{12} + RO_2^{\bullet} \longrightarrow c\text{-}C_6H_{11}^{\bullet} + RO_2H, \qquad (2)$$
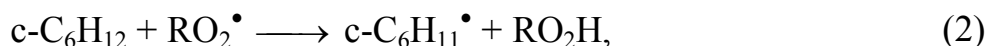
where $RO_2\bullet$ – cyclohexyl peroxyl radical.

The localization of the transition state (TS) of the reaction (2) was carried out in the approximation PM3 Unrestricted Hartree-Fock method. The starting geometry of the saddle point has been found by the method proposed in [3]. The saddle point on the potential energy surface corresponding to the TS, has been localized by Bartel method, realized in MOPAC 93. This saddle point was tested as follow. We performed a numerical harmonic vibrational analysis by calculation of the mass-weighted Hessian and obtained frequencies and forms of normal vibrations, one of which is imaginary and corresponds to the mode of the antisymmetric C<–>H–><–O vibration of atoms of the reaction center. Besides the reaction coordinate was built in mass-weighted Cartesian coordinates using the method of the internal reaction coordinate as shown in Figure 1.

Primary disturbance (equal to the quantum of vibrational energy) in the direction of the normal coordinate and reversible disturbance in the opposite direction to the normal coordinate has been applied. Thus, the internal reaction's coordinate was built from the transition state along the way down the reaction channels in both directions until the reactants and reaction products.
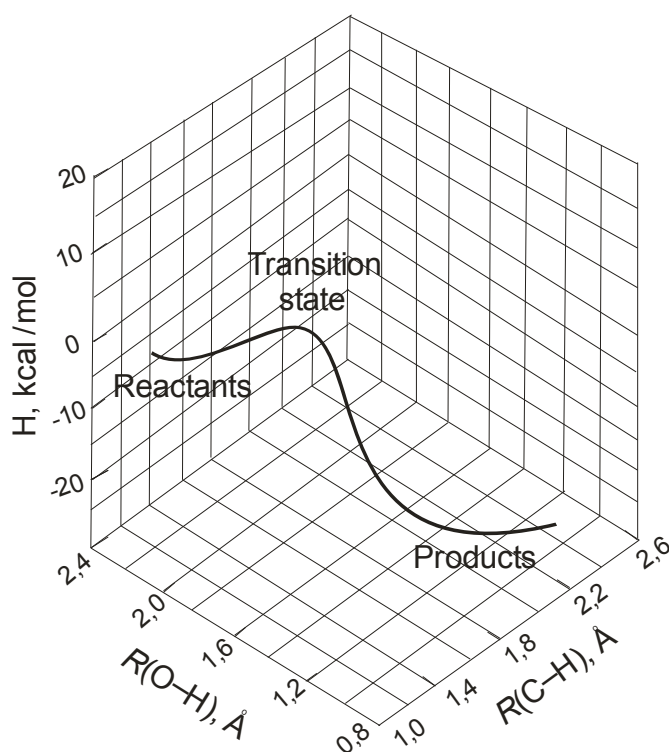
Figure 1 – Reaction (2) coordinate

Figure 1 shows that the transition state actually connects the reactants and products. The reduction of the potential energy of the system is monotonic in both directions on the way from the TS.

The values of the calculated parameters of the transition state of the reaction (2): the imaginary frequency *(v·I)*, the relative increase of the length of C–H and O–H bonds in the transition state *(ΔR)*, the total square of deformation of the bond lengths in the reactants and products in relation to the transition state (*r**), the total electronic charge on the fragments of TS are shown in the Table 1.

Table 1 – The values of the calculated parameters of the transition state of the reaction (2)

$v \cdot I$, $cм^{-1}$	ΔR_{C-H}, Å	ΔR_{O-H}, Å	r^*, Å^2		Electronic charge on the fragments of TS		
			Reactants	Products	c-C$_6$H$_{11}$	H	O$_2$R
1683	0,1119	0,2433	0.01	20,04	0,022	0,110	–0,132

As follows from the results, the transition state of the reaction is very close geometrically to the structure of the reactants and far away from products. This is evidenced by the small deformation of the TS structure from the structure of the reagents and a large deformation from the structure of the products. Most notable is the fact that the transition state of the reaction is polarized, i.e. the transfer of the electron density from the molecule containing the C–H bond to the peroxyl radical is observed. Thus, the reaction proceeds by the donor-acceptor mechanism, where the oxidize molecule is an electron donor, and the peroxyl radical is an acceptor.

It should be expected that there is a functional dependence between the electron-donor properties of the molecule (ionization energy, electron-charge distribution on the atoms of the reaction center) and the ability of the molecule to oxidize. The authors of [3] obtained a correlation as shown in Figure 2, which connect the activation energy of the reaction with the parameters of the electronic structure of the following reagents: c-C_6H_{12}, $PhCH_3$, PhC_2H_5, $PhCH(CH_3)_2$, 1,4-$(CH_3)_2C_6H_4$, 1,4-$(C_2H_5)_2C_6H_4$, 1,4-(изо-$C_3H_7)_2C_6H_4$, Ph_2CH_2, PhCHO:

$$E_a = 925{,}1 + 485{,}6 \cdot F_O - (78{,}1 \cdot F_H + 1{,}0 \cdot \delta_{cyk}), \tag{3}$$

where Q_H, Q_O – electronic charges on the atoms of the reaction center H and O;
I_{RH}, I_{RO2} – ionization potential of the molecule and peroxyl radical;
$F_O = (Q_O/I_{RO2})^{1/2}$ and $F_H = (Q_H/I_{RH})$;
$\delta_{cyk} = 0$ or 1 (depending on the presence or absence of a saturated cycle).
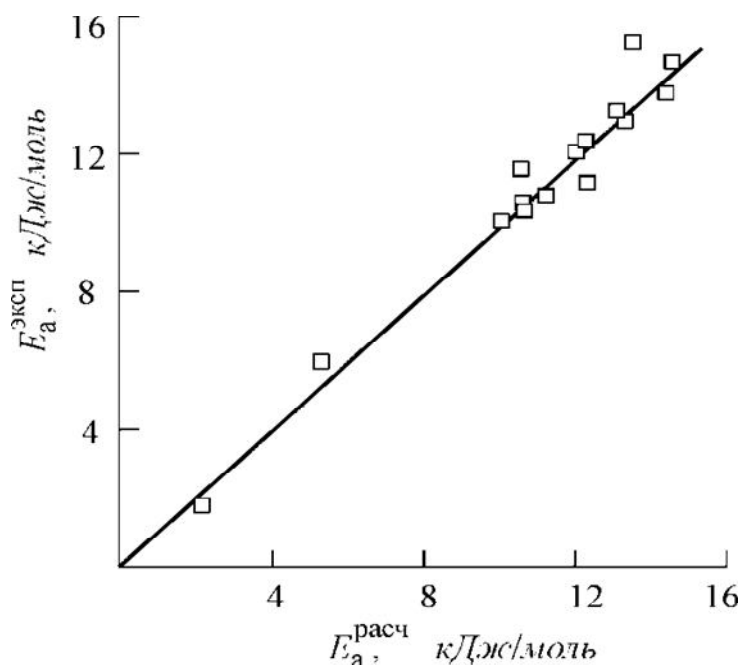

Figure 2 – The relationship between the experimental values of the activation energy and values of the activation energy calculated from equation (3), for the hydrogen abstraction by peroxyl radical

These results allow us to suggest that similar dependence should be observed for compounds with a more reactive X-H bond.

Based on this assumption, we calculated the electronic structure of a number of aromatic amines and phenols, for which the experimental values of the reaction rate constants at 60°C are known [4].

$$Ph(CH_3)_2COO^\bullet + InH \longrightarrow Ph(CH_3)_2COOH + In^\bullet. \tag{4}$$
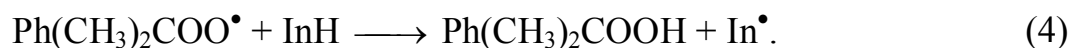
Following aromatic phenols and amines have been used as InH:

(XI)

(XII)

(XIII)

(XIV)

(XV)

(XVI)

(XVII)

(XVIII)

(XIX)

(XX)

(XXI)

(XXII)
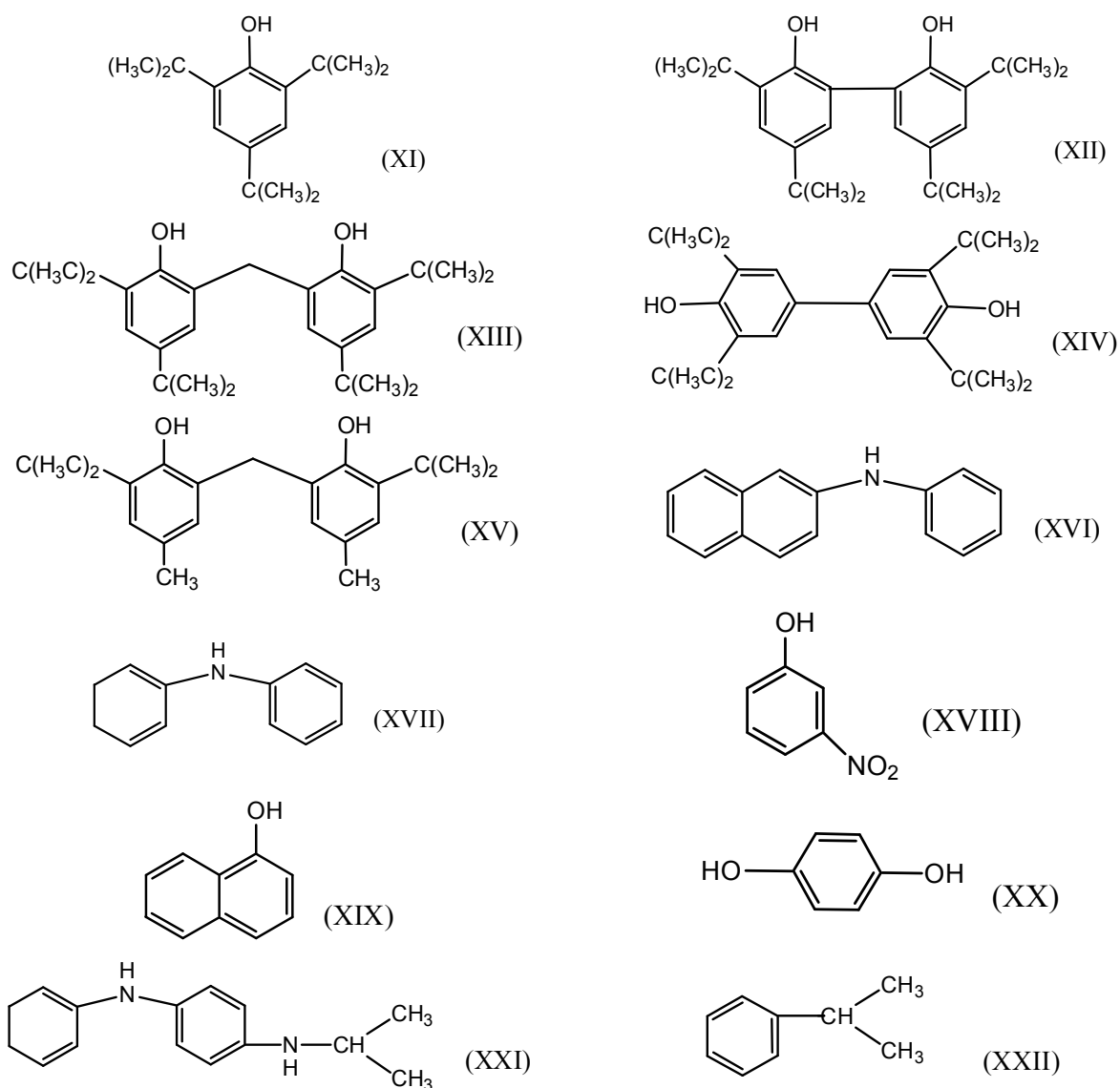
The results of the quantum-chemical calculations of these compounds are given in Table 2.

It should be noted in general, that the hydrogen abstraction from the X-H bond leads to radicals centered on the atom X. Radicals in which the unpaired electron is centered on C, O or N atoms are quite different the spin density localized on these atoms. Therefore, the oxidative capacity of molecules containing X-H bond will be determined not only by the electron-donating ability of the molecule, but also by the stability of the forming radical.

Accounting for this fact it was possible to obtain an equation relating the logarithm of the rate constant of reaction (4) with the electronic parameters of the reactants and reaction products:

$$\lg k = (24{,}3\pm2{,}0) - (102{,}1\pm10{,}4)F_H - (19{,}1\pm1{,}7)\rho_X + (1{,}1\pm0{,}2)n_{XH}, \qquad (5)$$

where ρ_X – the spin density on the atom X forming radical:
      n_{XH} – the number of reactive X-H bonds. Multiple correlation coefficient is 0,97 and the standard error is 0,4.

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Table 2 – *Values of the enthalpy of formation ($\Delta H_{f, 298}$), ionization potential (I), the charges on the H atom of the tearing X-H bond (Q_H) and the value of the spin density (ρ_X) on the atom X of the formed radical In• by the reaction of (5)*

Number of the substance	$\Delta H_{f, 298}$, kcal/mol	I, eV	Q_H	ρ_X
XI	−79,20	8,74	0,2111	0,2797
XII	−115,83	8,46	0,2111	0,2882
XIII	−129,90	8,65	0,2070	0,2999
XIV	−111,36	8,21	0,2164	0,2853
XV	−101,65	8,73	0,2065	0,3009
XVI	67,75	8,33	0,0508	0,6724
XVII	50,50	8,60	0,049	0,6840
XVIII	−30,14	9,99	0,2042	0,3608
XIX	−3,28	8,54	0,1994	0,2573
XX	−66,25	8,75	0,1953	0,3192
XXI	35,91	8,20	0,0482	0,6770
XXII	5,35	9,44	0,0659	0,9098

Conclusions. Our results demonstrate that the ability of molecules to act as antioxidatants is determined first by their electron-donor properties, and, second, by a stability of the radical formed in the breaking of the X-H bond.

Список літератури / References:

1. Филатова И.А. Значение в профилактике заболеваний фенольных соединений плодов и ягод / И.А. Филатова, А.Ю. Колеснов // Пищевая промышленность. – 2000. – № 8. – С. 35-37.
   Filatova, I.A. and Kolesnov, A.Yu. (2000), "Importance of the phenolic compounds of fruits and berries in the prevention of diseases", *Pishchevaya promyshlennost,* no. 8, pp. 35-37.
2. Денисов Е.Т. Химическая кинетика / Е.Т. Денисов, О.М. Саркисов, Г.И. Лихтенштейн. – М.: Химия, 2000. – 568 с.
   Denisov, Ye.T., Sarkisov, O.M. and Likhtenshteyn, G.I. (2000), *Khimicheskaya kinetika* [Chemical Kinetics], Khimiia, Moscow, Russia.
3. Опейда И.А. Реакционная способность С–Н связи органических молекул различного строения в реакциях отрыва атома водорода пероксильными радикалами / И.А. Опейда, А.Ф. Дмитрук, О.М. Заречная // Теор. и эксперимент. химия. – 1997. – Т. 33. – № 1. – С. 6-11.
   Opeyda, I.A., Dmitruk, A.F and Zarechnaya, O.M. (1997), "The reactivity of the C–H bond of organic molecules with different structures in the reactions of hydrogen atom abstraction by peroxyl radicals", *Teor. i eksperiment. khimiia*, vol. 33, no. 1, pp. 6-11.
4. Ground states of molecules. 25. PM3 an improved version of the MNDO semiempirical SCF-MO method / M.J.S. Dewar, E.G. Zoebisch, E.F. Hedy, J.J.P. Stewart // J. Am. Chem. Soc. – 1985. – Vol. 10, № 7. – P. 3902-3912.

Dewar, M.J.S., Zoebisch, E.G., Hedy, E.F. and Stewart, J.J.P. (1985), "Ground states of molecules. 25. PM3 an improved version of the MNDO semiempirical SCF-MO method", *J. Am. Chem. Soc.*, vol. 10, no. 7, pp. 3902-3912.

5. Шляпников Ю.А. Антиокислительная стабилизация полимеров / Ю.А. Шляпников, С.Г. Кирюшкин, А.П. Марьин. – М.: Химия, 1986. – 256 с.

Shliapnikov, Yu.A., Kiriushkin, S.G. and Marin, A.P. (1986), *Antiokislitelnaya stabilizatsiya polimerov* [Antioxidative stabilization of polymers], Khimiia, Moscow, Russia.

Цель. В данной работе представлены результаты исследований электронного строения ряда органических молекул, содержащих O–H и N–H связи. Получены поверхности потенциальной энергии реакции отрыва атома H от этих молекул пероксильным радикалом.

Методика. Квантово-химические расчеты производились методом самосогласованного поля молекулярных орбиталей Хартри-Фока в приближении полуэмпирического метода PM3.

Результаты. На поверхности потенциальной энергии локализованы точки, соответствующие структурам переходных состояний, и оценены активационные параметры изученных реакций, установлены их электронные и геометрические характеристики. Рассчитаны электронные и термодинамические параметры природных антиоксидантов – ароматических аминов и фенолов.

Научная новизна. Получено уравнение, связывающее активационные параметры реакции с электронными характеристиками исходных реагентов. Установлено, что антиоксидантная активность вещества определяется электронно-донорными свойствами вещества и стабильностью образующегося радикала.

Практическая значимость. Полученные результаты дают возможность прогнозировать антиоксидантную способность различных ингибиторов природного происхождения.

Ключевые слова: *антиоксидантное действие, окисление пероксильным радикалом, фенольные соединения, гетероциклические молекулы, метод Хартри-Фока, константа скорости, энергия активации, электронные параметры.*

Мета. У роботі представлено результати досліджень електронної будови ряду органічних молекул, що містять O–H та N–H зв'язки. Отримано поверхні потенційної енергії реакції відриву атома Гідрогену від цих молекул пероксильним радикалом.

Методика. Квантово-хімічні розрахунки виконано за допомогою методу самоузгодженого поля молекулярних орбіталей Хартрі-Фока у наближенні напівемпіричного методу PM3.

Результати. На поверхні потенційної енергії було локалізовано точки, відповідні до структур перехідних станів, та оцінено активаційні параметри вивчених реакцій, встановлено їхні електронні та геометричні характеристики. Розраховано електронні та термодинамічні параметри природних антиоксидантів – ароматичних амінів і фенолів.

Наукова новизна. Одержано рівняння, що пов'язує активаційні параметри реакції з електронними характеристиками вихідних реагентів. Встановлено, що антиоксидантна активність речовини визначається електронно-донорними властивостями речовини та стабільністю радикала, що утворюється.

Практична значущість. Отримані результати дають можливість прогнозувати антиоксидантну здатність різних інгібіторів природного походження.

Ключові слова: *антиоксидантна дія, окислення пероксильним радикалом, фенольні сполуки, гетероциклічні молекули, метод Хартрі-Фока, константа швидкості, енергія активації, електронні параметри.*