Reactivity of Natural Phenols in Radical Reactions

T. G. Denisova and E. T. Denisov

Institute of Problems of Chemical Physics, Russian Academy of Sciences, Chernogolovka, Moscow oblast, 142432 Russia
e-mail: det@icp.ac.ru
Received February 29, 2008

Abstract—Activation enthalpies and energies and the rate constants of reactions with peroxyl, alkyl, and thiyl radicals (76 reactions) were calculated for a group of natural antioxidants (19 monohydroxy and polyhydroxy phenols). The calculation was performed with the use of the model of a radical abstraction reaction as the intersection of two parabolic potential curves. The results of the calculation were compared with experimental data: the average discrepancy in the activation energies of the reactions $RO_2^\bullet$ + ArOH was 0.8 kJ/mol. Interatomic distances in the reaction centers of the transition states of the test reactions were calculated. Factors affecting the reactivity of these compounds are discussed.

DOI: 10.1134/S002315840903001X

INTRODUCTION

Natural antioxidants are in wide current use as food additives; they have been intensively studied in the past quarter of a century [1–6]. The efficiency of their action is primarily related to their antiradical activity. Among radical reactions, only the reactions of alkylperoxyl radicals with a small number of natural phenols have been studied in sufficient detail [7, 8]. Reactions of alkyl and thiyl radicals have received little attention [8]. Recently, we calculated the dissociation energies of O–H bonds for a great number (64) of biological antioxidants [9]. This provided an opportunity to calculate activation energies (E) and rate constants (k) for the reactions of various free radicals and molecules with biological antioxidants. This paper is devoted to this problem. The mathematical apparatus and kinetic parameters of the method of intersecting parabolas were used in the calculation [1, 7, 10, 11].

Here, we consider the radical reactions that are of undoubted interest for the kinetic analysis of the efficiency of action of biological oxidants. First, these are the reactions of phenols with peroxyl radicals. Note that not only the lipid radicals $RO_2^\bullet$, which are close to alkylperoxyl radicals in terms of activity, but also $RO_2^\bullet$ containing various functional groups are formed in the body. α-Hydroxyperoxyl radicals, which rapidly decompose with the formation of $HO_2^\bullet$, are generated from sugars. For example, acylperoxyl and α-ketoperoxyl radicals are formed from glucose and fructose, respectively. Thus, in this study, we calculated the activation energies E and rate constants k for both the reactions of alkylperoxyl radicals with biological antioxidants and $RO_2^\bullet$ with various functional groups. Second, carbon-centered radicals appear in the body, and these

radicals react with biological antioxidants. We consider the reactions of the most active secondary alkyl radical generated from lipids. Third, the thiyl group occurs in proteins as a constituent of the L-cysteine residue; this group forms a thiyl radical by a reaction with any radical. Therefore, we also consider the reactions of thiyl radicals with biological antioxidants. In addition to kinetic characteristics, we calculated interatomic distances in the reaction centers of the transition states in accordance with a previously developed procedure [12, 13].

CALCULATION

The classical enthalpy ΔH_e of the abstraction reaction

$$X^\bullet + ArOH \longrightarrow XH + ArO^\bullet$$
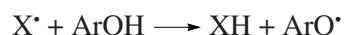
was calculated as the difference of dissociation energies of cleaved and formed bonds with consideration for their zero-point vibration energies:

$$\Delta H_e = D(ArO–H) – D(X–H) + 0.5hN_A\Delta\nu, \quad (1)$$

where the last term is the difference between the zero-point vibration energies of reacting bonds (h is Planck's constant, N_A is Avogadro's number, and $\Delta\nu$ is the difference between the stretching vibration frequencies of O–H and X–H bonds). Table 1 summarizes the list of natural phenols chosen for calculations, the numbers of equireactive phenol groups $n_{O–H}$, and the strengths of the weakest bonds $D_{O–H}$ [9]. The dissociation energies of O–H bonds in hydroperoxides were taken from [14]; $D_{C–H}(sec-R–H) = 412$ kJ/mol [15], and $D_{S–H}(cysteine) = 360.0$ kJ/mol [16].

The activation energies of the reactions of free radicals with phenols were calculated using the method of intersecting parabolas [1, 7, 10, 11]. This method is

Table 1. Structural formulas of natural antioxidants, dissociation energies of reactive O–H bonds (D_{O-H}) (kJ/mol) [9], and numbers of the most reactive O–H groups (n_{O-H})
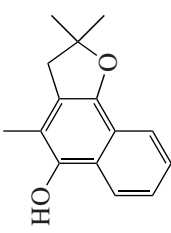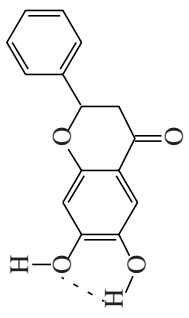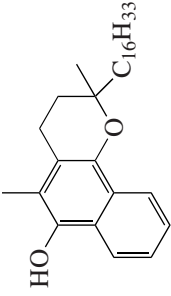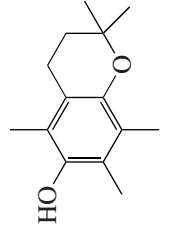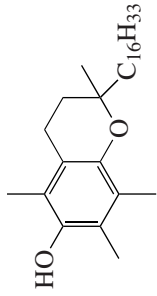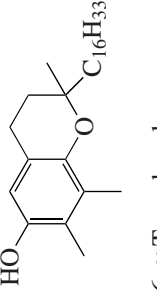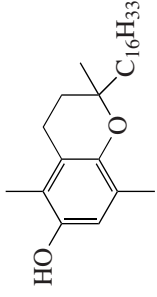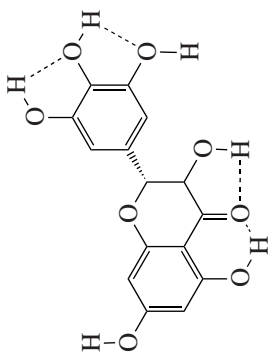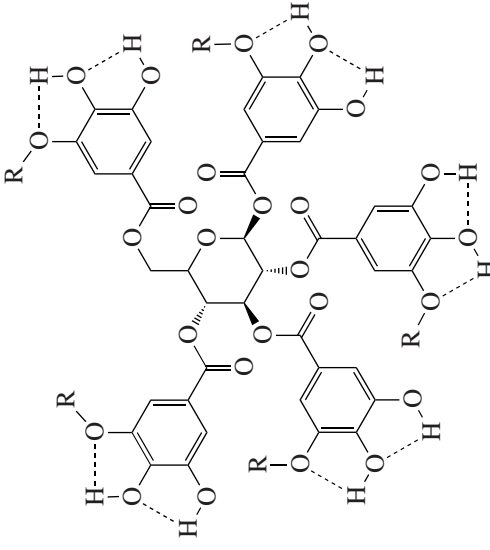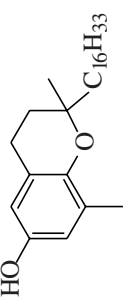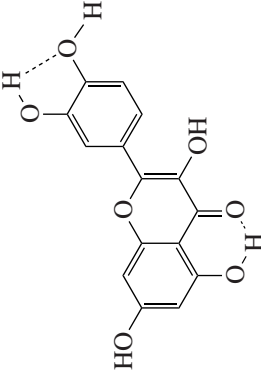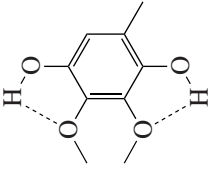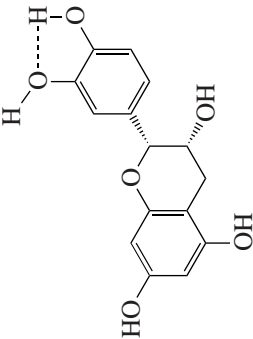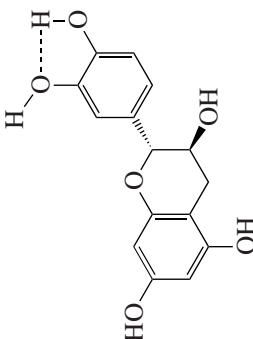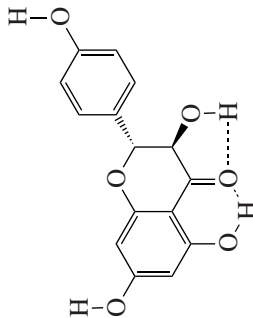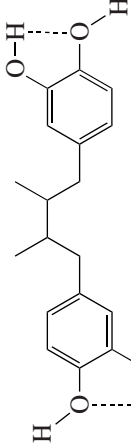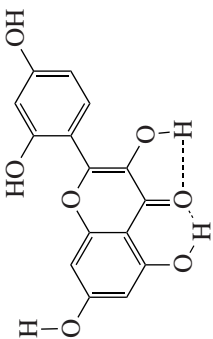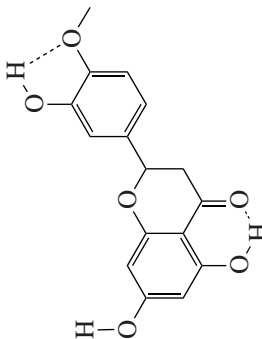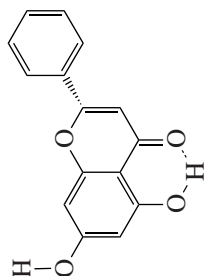
1. Naphtho[1,2-b]furan, 2,3-dihydro-2,2,4-trimethyl-5-hydroxy-, $D_{O-H} = 315.3$

2. 7,8-Benzochromane, 2,5-dimethyl-2-phytyl-6-hydroxy-, $D_{O-H} = 321.4$

3. Chromane, 2,2,5,7,8-pentamethyl-6-hydroxy-, $D_{O-H} = 328.4$

4. α-Tocopherol, $D_{O-H} = 330.0$

5. 6,7-Dihydroxyflavone, $n_{O-H} = 1$, $D_{O-H} = 332.3$

6. γ-Tocopherol, $D_{O-H} = 334.9$

7. β-Tocopherol, $D_{O-H} = 335.3$

8. Tannic acid, R = gallate, $n_{O-H} = 5$, $D_{O-H} = 338.1$

9. Myricetin, $n_{O-H} = 1$, $D_{O-H} = 340.9$

Table 1. (Contd.)

13. (–)-Epicatechol,
$n_{O-H} = 1$, $D_{O-H} = 346.2$

12. Ubiquinol-0,
$n_{O-H} = 2$, $D_{O-H} = 345.2$

16. Nordihydroguaiaretic acid,
$n_{O-H} = 2$, $D_{O-H} = 351.3$

19. Morin, $n_{O-H} = 2$, $D_{O-H} = 363.6$

11. Quercetin,
$n_{O-H} = 1$, $D_{O-H} = 343.0$

15. Kaempferol,
$n_{O-H} = 2$, $D_{O-H} = 348.9$

18. Crysin,
$n_{O-H} = 1$, $D_{O-H} = 357.1$

10. δ-Tocopherol
$D_{O-H} = 341.5$

14. Catechin,
$n_{O-H} = 1$, $D_{O-H} = 348.1$

17. Hesperetin,
$n_{O-H} = 1$, $D_{O-H} = 353.8$

valid for reactions occurring in a nonpolar solvent, which does not form hydrogen bonds with phenol. The classical potential barrier of reaction E_e is calculated through the classical enthalpy ΔH_e.

For reactions with the coefficient $\alpha = 1$, E_e is calculated from the equation

$$\sqrt{E_e} = \frac{br_e}{2} + \frac{\Delta H_e}{2br_e}; \qquad (2)$$

for reactions with the coefficient α close to unity, E_e is calculated from the equation

$$\sqrt{E_e} = \frac{br_e}{1+\alpha} + \frac{\alpha \Delta H_e}{2br_e}, \qquad (3)$$

whereas it is calculated from the following equation for reactions with the coefficient α different from unity:

$$\sqrt{E_e} = \frac{br_e}{1-\alpha^2}\left\{1 - \alpha\sqrt{1 - \frac{1-\alpha^2}{(br_e)^2}\Delta H_e}\right\}. \qquad (4)$$

The coefficient α^2 is the ratio between the force constants of ArO–H and X–H bonds; $2b^2$ is the force constant of the O–H bond of phenol; and r_e is the total elongation of ArO–H and X–H bonds in the transition state, as calculated from experimental data using the method of intersecting parabolas. For phenols, $b = 46.65 \times 10^{10}$ kJ$^{1/2}$ mol$^{-1/2}$ m^{-1}, $0.5hN_A\nu_{ArO-H} = 21.5$ kJ/mol, and ν_{ArO-H} is the stretching vibration frequency of the O–H bond [7]. The activation energy of reaction was calculated from E_e by the equation

$$E = E_e - 0.5hN_A\nu_{ArO-H} + 0.5RT. \qquad (5)$$

Equations (2)–(4) are valid if ΔH_e of reaction varies within the range of $\Delta H_{e,\,min} < \Delta H_e < \Delta H_{e,\,max}$ [10]; this took place for all of the test reactions. The rate constant of a radical reaction was calculated from the Arrhenius equation

$$k = n_{O-H}A\exp(-E/RT). \qquad (6)$$

Each particular class of radical reactions is characterized by a reaction center and constant values of ν_{O-H}, ν_{X-H}, br_e, and A, as well as the classical potential barrier $E_{e,\,0}$, which is calculated from the equation [10]

$$E_{e,\,0} = \{br_e/(1+\alpha)\}^2. \qquad (7)$$

For the class of the reactions R$^\bullet$ + ArOH $\longrightarrow$ ArO$^\bullet$ + RH, where RH is an aliphatic hydrocarbon, the parameter br_e was calculated in this work from experimental data as described below. Previously [17, 18], the reaction rate constant of the alkyl radical 5-hexenyl with α-tocopherol was measured using the method of competitive reactions. The dissociation energy of a C–H bond in the methyl group of a paraffin is 422 kJ/mol [7]; consequently, the enthalpy of this reaction is $\Delta H = -92.0$ kJ/mol, and $\Delta H_e = -87.9$ kJ/mol. As calculated from Eq. (6), the activation energy of this reaction is 11.6 [17] or 11.1 kJ/mol [18]; the average value is $E = $

11.4 kJ/mol, and $E_e = 31.6$ kJ/mol. We calculate the parameter br_e from the equation [10]

$$br_e = \alpha(E_e - \Delta H_e)^{1/2} + E_e^{1/2}, \qquad (8)$$

where $\alpha = 1.247$. We obtain $br_e = 19.25$ kJ$^{1/2}$ mol$^{-1/2}$.

For the class of the reactions RS$^\bullet$ + HOAr, experimental data are not available. Therefore, we evaluated the parameter br_e for this class of reactions through an analogous parameter for the reaction RO$_2^\bullet$ + ArSH with a structurally similar reaction center. For this reaction, $br_e = 12.38$ kJ$^{1/2}$ mol$^{-1/2}$ [16] and $r_e = 0.373 \times 10^{-10}$ m^{-1}; for the reaction RS$^\bullet$ + HOAr, we obtain $br_e = 46.65 \times 10^{10} \times 0.373 \times 10^{-10} = 17.40$ kJ$^{1/2}$ mol$^{-1/2}$. For other classes of reactions, these parameters were taken from a handbook [7].

Previously [12, 13], a simple procedure was developed for calculating interatomic distances in the reaction center of a transition state from the enthalpy and activation energy of the reaction by combining the results obtained by quantum-chemical calculations and using the method of intersecting parabolas. This procedure allowed us to calculate interatomic distances in the transition state of a reaction, which coincided with those calculated using the density functional theory. As applied to the test reactions, interatomic distances were calculated by this procedure in accordance with the following equations:

$$r^{\neq}_{ArO-H} = r_{ArO-H} + \beta b^{-1}\sqrt{E_e}; \qquad (9)$$

$$r^{\neq}_{X-H} = r_{X-H} + a\beta b^{-1}\sqrt{E_e - \Delta H_e}. \qquad (10)$$

The interatomic distances in molecules were [19] $r_{O-H} = 0.967 \times 10^{-10}$ m, $r_{C-H} = 1.092 \times 10^{-10}$ m, and $r_{S-H} = 1.340 \times 10^{-10}$ m; the normalization factors β were taken from [13]. Table 2 summarizes the kinetic parameters and coefficients for the chosen classes of reactions.

RESULTS AND DISCUSSION

Table 3 summarizes the calculated enthalpies, activation energies, and rate constants of reactions of alkylperoxyl radicals with a number of natural antioxidants (see Table 1). The interatomic distances $r^{\neq}(ArO...H)$ and $r^{\neq}(ROO...H)$ for the transition states of these reactions are also given in Table 3. All of the test reactions are exothermic (ΔH varied over the range from –50 to –2 kJ/mol); their activation energies varied from 1 to 22 kJ/mol, and $k(310\text{ K})$ varied from 1.4×10^4 to 1.9×10^7 1 mol^{-1} s^{-1}. As the reaction enthalpy increased, the distance $r^{\neq}_{ArO...H}$ increased, whereas $r^{\neq}_{ROO...H}$ decreased.

Table 4 summarizes the calculated values of ΔH, E, and k for the reactions of structurally different peroxyl radicals with α-tocopherol. The reactions of two peroxyl radicals, namely, RC(O)OO$^\bullet$ and PhC(O)OO$^\bullet$, are

Table 2. Kinetic parameters of the reactions of $R^{\bullet}$, $RO_2^{\bullet}$, and $RS^{\bullet}$ radicals with natural phenols [7, 12, 13, 16]

Reaction class	α	β	$0.5hN_A\Delta\nu$, kJ/mol	br_e, kJ$^{1/2}$ mol$^{-1/2}$	A_0, l mol^{-1} s^{-1}	$-\Delta H_{e,\,min}$, kJ/mol	$\Delta H_{e,\,max}$, kJ/mol
$RO_2^{\bullet} + Ar_iOH$	1.014	1.49	0.3	13.16	3.20×10^7	49.1	53.6
$R^{\bullet} + Ar_iOH$	1.247	1.44	4.1	19.25	1.00×10^8	115.8	272.8
$RS^{\bullet} + Ar_iOH$	1.405	1.39	6.4	17.40	1.00×10^8	61.1	127.5

Table 3. Enthalpies, activation energies, rate constants, and interatomic distances $r^{\neq}_{ArO-H}$ and $r^{\neq}_{ROO-H}$ for the reactions sec-$RO_2^{\bullet} + Ar_iOH \longrightarrow sec$-$RO_2H + Ar_iO^{\bullet}$ with natural phenols, as calculated from Eqs. (1), (3), (5), (6), (9), and (10) ($D_{ROO-H} = 365.5$ kJ/mol; $A_0 = 3.20 \times 10^7$ l mol^{-1} s^{-1}, $T = 310$ K)

Ar_iOH	$-\Delta H_e$, kJ/mol	E, kJ/mol	k, l mol^{-1} s^{-1}	$r^{\neq}_{ArO-H} \times 10^{10}$, m	$r^{\neq}_{ROO-H} \times 10^{10}$, m
Naphtho[1,2-*b*]furan, 2,3-dihydro-5-hydroxy-2,2,4-trimethyl-	49.9	1.3	1.93×10^7	1.114	1.240
7,8-Benzochromane, 6-hydroxy-2,5-dimethyl-2-phytyl-	43.8	3.3	8.92×10^6	1.122	1.233
Chromane, 2,2,5,7,8-pentamethyl-6-hydroxy-	36.8	6.0	3.15×10^6	1.130	1.224
α-Tocopherol	35.2	6.6	2.46×10^6	1.132	1.222
6,7-Dihydroxyflavone	32.9	7.5	1.72×10^6	1.135	1.219
γ-Tocopherol	30.3	8.6	1.14×10^6	1.138	1.216
β-Tocopherol	29.9	8.8	1.07×10^6	1.139	1.215
Tannic acid	27.1	9.9	3.38×10^6	1.142	1.212
Myricetin	24.3	11.1	4.25×10^5	1.146	1.209
δ-Tocopherol	23.7	11.4	3.84×10^5	1.147	1.208
Quercetin	22.2	12.1	2.98×10^5	1.148	1.206
Ubiquinol-0	20.0	13.0	4.10×10^5	1.151	1.203
(–)-Epicatechol	19.0	13.5	1.72×10^5	1.152	1.202
Catechin	17.1	14.3	1.24×10^5	1.155	1.200
Kaempferol	16.3	14.7	2.15×10^5	1.156	1.199
Nordihydroguaiaretic acid	13.9	15.8	1.40×10^5	1.159	1.196
Hesperetin	11.4	17.0	4.46×10^4	1.162	1.193
Crysin	8.1	18.5	2.43×10^4	1.166	1.189
Morin	1.6	21.7	1.42×10^4	1.174	1.181

exothermic so that their enthalpies $\Delta H_e < \Delta H_{e,\,min}$. Therefore, their activation energy is $0.5RT$. Depending on the strength of the ROO–H bond, the enthalpies of these reactions vary within the range from –74 to –28 kJ/mol and activation energies vary within the range of 1.3–9.5 kJ/mol.

Table 5 summarizes the results of a comparison between the activation energies of the reactions of peroxyl radicals with natural phenols calculated using the method of intersecting parabolas and the experimental activation energies. These latter were calculated from rate constants using the Arrhenius equation $E_{expt} =$

Table 4. Enthalpies, activation energies, rate constants, and interatomic distances $r_{ArO-H}^{\neq}$ and $r_{ROO-H}^{\neq}$ for the reactions $R_iO_2^{\cdot} + TcOH \longrightarrow R_iOOH + TcO^{\cdot}$, as calculated from Eqs. (1), (3), (5), (6), (9), and (10) (TcOH is α-tocopherol; $D_{TcO-H} = 330.0$ kJ/mol, $A_0 = 3.20 \times 10^7$ l mol^{-1} s^{-1}, $T = 310$ K)

$R_iO_2^{\cdot}$	D_{ROO-H}, kJ/mol	$-\Delta H_e$, kJ/mol	E, kJ/mol	k, l mol^{-1} s^{-1}	$r_{ArO-H}^{\neq} \times 10^{10}$, m	$r_{ROO-H}^{\neq} \times 10^{10}$, m
$HO_2^{\cdot}$	369.0	38.7	5.2	4.20×10^6	1.128	1.226
$R_2CHO_2^{\cdot}$	365.5	35.2	6.6	2.46×10^6	1.132	1.222
$R_3CO_2^{\cdot}$	358.6	28.3	9.4	8.22×10^5	1.141	1.214
$cyclo$-[(CH$_2$)$_5$C(OH)OO$^{\cdot}$]	362.1	31.8	8.0	1.44×10^6	1.137	1.218
$RPhC(OH)OO^{\cdot}$	359.8	29.5	8.9	9.99×10^5	1.139	1.215
$ROCH(OO^{\cdot})R$	367.3	37.0	5.9	3.24×10^6	1.130	1.224
$R_2CHOC(OO^{\cdot})R_2$	358.4	28.1	9.5	7.96×10^5	1.141	1.213
$ROCH(OO^{\cdot})Ph$	374.8	44.5	3.0	9.87×10^6	1.121	1.234
$cyclo$-[(CH$_2$)$_3$OCHOO$^{\cdot}$]	367.6	37.3	5.8	3.40×10^6	1.130	1.225
$RC(O)OO^{\cdot}$	387.1	56.8	1.3	3.49×10^7	1.106	1.249
$R_3CC(O)OO^{\cdot}$	376.9	46.6	2.3	1.33×10^7	1.118	1.236
$PhC(O)OO^{\cdot}$	403.9	73.6	1.3	4.00×10^8	1.106	1.320
$RC(O)CRHOO^{\cdot}$	369.8	39.5	4.9	4.74×10^6	1.127	1.227
$RC(O)OCPhHOO^{\cdot}$	376.4	46.1	2.4	1.24×10^7	1.119	1.236

Table 5. Comparison between experimental activation energies E_{expt} and theoretical activation energies E_{calcd} (calculated from Eqs. (1), (2), and (5)) for the reactions $RO_2^{\cdot} + Ar_iOH \longrightarrow ROOH + Ar_iO^{\cdot}$

Ar_iOH	D_i, kJ/mol	E_{expt}, kJ/mol	E_{calcd}, kJ/mol	ΔE, kJ/mol	References
Naphtho[1,2-b]furan, 2,3-dihydro-5-hydroxy-2,2,4-trimethyl-	315.3	0.3	1.1	0.8	[20]
7,8-Benzochromane, 6-hydroxy-2,5-dimethyl-2-phytyl-	321.4	2.6	3.3	0.7	[20]
Chromane, 2,2,5,7,8-pentamethyl-6-hydroxy-	328.4	5.4	6.0	0.6	[20]
α-Tocopherol	330.0	5.8; 6.1; 7.4; 5.9	6.6	0.7 ± 0.1	[4, 6, 20, 21]
γ-Tocopherol	334.9	7.9	8.6	0.7	[4]
β-Tocopherol	335.3	8.1	8.8	0.7	[4]
δ-Tocopherol	341.5	10.8	11.4	0.6	[4]
Quercetin	343.0	11.6; 12.5	12.1	0.4 ± 0.05	[21, 22]
Ubiquinol-0	345.2	14.1	13.0	1.1	[21]
Ubiquinol-2	345.2	14.3	13.0	1.3	[21]
Ubiquinol-6	345.2	14.3	13.0	1.3	[21]
Ubiquinol-9	345.2	13.9	13.0	0.9	[21]
Ubiquinol-10	345.2	14.1	13.0	1.1	[21]
(−)-Epicatechol	346.2	11.7	13.5	1.8	[22]
Crysin	357.1	19.2	18.5	0.7	[23]
Catechin	348.1	15.2	14.3	0.9	[24]

Table 6. Enthalpies, activation energies, rate constants, and interatomic distances $r^{\neq}_{\text{ArO–H}}$ and $r^{\neq}_{\text{C–H}}$ for the reactions $sec\text{-}R^{\bullet}$ + $Ar_iOH \longrightarrow RH + Ar_iO^{\bullet}$, as calculated from Eqs. (1), (4), (5), (6), (9), and (10) ($D_{\text{R–H}} = 412.0$ kJ/mol; $A_0 = 1.00 \times 10^8$ l mol^{-1} s^{-1}, $T = 310$ K)

Ar_iOH	$-\Delta H_e$, kJ/mol	E, kJ/mol	k, l mol^{-1} s^{-1}	$r^{\neq}_{\text{ArO–H}} \times 10^{10}$, m	$r^{\neq}_{\text{C–H}} \times 10^{10}$, m
Naphtho[1,2-*b*]furan, 2,3-dihydro-5-hydroxy-2,2,4-trimethyl-	92.6	9.5	2.52×10^6	1.135	1.518
7,8-Benzochromane, 6-hydroxy-2,5-dimethyl-2-phytyl-	86.5	11.9	1.01×10^6	1.142	1.511
Chromane, 2,2,5,7,8-pentamethyl-6-hydroxy-	79.5	14.7	3.39×10^5	1.149	1.504
α-Tocopherol	77.9	15.3	2.63×10^5	1.151	1.502
6,7-Dihydroxyflavone	75.6	16.3	1.82×10^5	1.153	1.499
γ-Tocopherol	73.0	17.4	1.19×10^5	1.156	1.497
β-Tocopherol	72.6	17.5	1.12×10^5	1.157	1.496
Tannic acid	69.8	18.7	3.52×10^5	1.160	1.493
Myricetin	67.0	19.9	4.41×10^4	1.163	1.490
δ-Tocopherol	66.4	20.2	3.99×10^4	1.163	1.490
Quercetin	64.9	20.8	3.10×10^4	1.165	1.488
Ubiquinol-0	62.7	21.8	4.26×10^4	1.167	1.486
(–)-Epicatechol	61.7	22.2	1.79×10^4	1.168	1.485
Catechin	59.8	23.1	1.29×10^4	1.170	1.483
Kaempferol	59.0	23.4	2.25×10^4	1.171	1.482
Nordihydroguaiaretic acid	56.6	24.5	1.48×10^4	1.173	1.479
Hesperetin	54.1	25.7	4.74×10^3	1.176	1.477
Crysin	50.8	27.2	2.63×10^3	1.179	1.473
Morin	44.3	30.2	1.60×10^3	1.186	1.467

$RT\ln(n_{\text{O–H}}A_0/k)$. The column $\Delta E = |E - E_{\text{expt}}|$ indicates that the calculated values and experimental data are consistent (the average discrepancy between E_{calcd} and E_{expt} is $\Delta E = 0.8 \pm 0.3$ kJ/mol.

Not only peroxyl radicals but also alkyl radicals react with antioxidants. In lipids, secondary alkyl radicals appear under the action of radicals from fatty acid residues. Table 6 summarizes the values of ΔH_e, E, and k and interatomic distances in the transition states of reactions between this radical and natural antioxidants, as calculated from Eqs. (1), (4)–(6), (9), and (10). It can be seen that the reactions of an alkyl radical with phenols are highly exothermic; their ΔH varies over the range of –97 to –48 kJ/mol, the activation energy varies from 9 to 30 kJ/mol, and the rate constant (at $T = 310$ K) changes from 1.6×10^3 to 2.5×10^6 l mol^{-1} s^{-1}.

The reactions of thiyl radicals with biological antioxidants are exothermic for the most part (Table 7). Their activation energies vary within the range of 12–38 kJ/mol, and $k(310$ K) vary from 38 to 1.1×10^6 l mol^{-1} s^{-1}. There is no experimental data on these reactions.

The above data indicate that the enthalpy of reaction plays a decisive role in the formation of activation energy; in turn, the enthalpy of reaction depends on the strengths of the attacked bond in phenol and the resulting X–H bond. In addition to this important factor, there are a number of other factors affecting the formation of an activation barrier [10]. The occurrence of these factors follows from a comparison between classical potential barriers $E_{e,0}$ (see Eq. (7)) for various classes of reactions. The above classes of reactions are arranged in the following order of increasing classical potential barriers of thermally neutral reactions: $E_{e,0}$ (kJ/mol) = 42.7 ($RO_2^{\bullet}$, O_2, O_3 + Ar_iOH) < 50.8 ($RS^{\bullet}$ + Ar_iOH) < 61.4 ($R^{\bullet}$ + Ar_iOH). It can be seen that the radicals and molecules that attack phenol are also dramatically different in activation energies at $\Delta H_e = 0$. This difference in the activities of the above radicals is due to the following factors.

(1) In addition to enthalpy, triplet repulsion, which increases the activation barrier [10], affects the activation energy. This triplet repulsion is due to the fact that

Table 7. Enthalpies, activation energies, rate constants, and interatomic distances $r^{\neq}_{ArO-H}$ and $r^{\neq}_{RS-H}$ for the reactions $RS^{\bullet} + Ar_iOH \longrightarrow RSH + Ar_iO^{\bullet}$, as calculated from Eqs. (1), (4), (5), (6), (9), and (10) ($RS^{\bullet}$ is the thiyl radical of L-cysteine; $D_{RS-H} = 360$ kJ/mol; $A_0 = 1.00 \times 10^8$ l mol^{-1} s^{-1}; $T = 310$ K)

Ar_iOH	ΔH_e, kJ/mol	E, kJ/mol	k, l mol^{-1} s^{-1}	$r^{\neq}_{ArO-H} \times 10^{10}$, m	$r^{\neq}_{RS-H} \times 10^{10}$, m
Naphtho[1,2-b]furan, 2,3-dihydro-5-hydroxy-2,2,4-trimethyl-	−38.3	11.6	1.12×10^6	1.135	1.690
7,8-Benzochromane, 6-hydroxy-2,5-dimethyl-2-phytyl-	−32.2	14.6	3.46×10^5	1.143	1.683
Chromane, 2,2,5,7,8-pentamethyl-6-hydroxy-	−25.2	18.2	8.61×10^4	1.152	1.674
α-Tocopherol	−23.6	19.0	6.22×10^4	1.154	1.672
6,7-Dihydroxyflavone	−21.3	20.3	3.88×10^4	1.156	1.669
γ-Tocopherol	−18.7	21.6	2.26×10^4	1.160	1.666
β-Tocopherol	−18.3	21.9	2.08×10^4	1.160	1.665
Tannic acid	−15.5	23.4	1.15×10^4	1.164	1.662
Myricetin	−12.7	24.9	6.34×10^3	1.167	1.658
δ-Tocopherol	−12.1	25.3	5.57×10^3	1.168	1.658
Quercetin	−10.6	26.1	4.03×10^3	1.170	1.656
Ubiquinol-0	−8.4	27.3	2.49×10^3	1.172	1.653
(−)-Epicatechol	−7.4	27.9	2.00×10^3	1.174	1.652
Catechin	−5.5	29.0	1.32×10^3	1.176	1.650
Kaempferol	−4.7	29.4	1.10×10^3	1.177	1.649
Nordihydroguaiaretic acid	−2.3	30.8	6.45×10^2	1.180	1.646
Hesperetin	0.2	32.3	3.67×10^2	1.183	1.643
Crysin	3.5	34.2	1.73×10^2	1.187	1.639
Morin	10.0	38.1	3.80×10^1	1.195	1.631

one of the three electrons of a reaction center occupies the nonbonding orbital; the stronger the ArO–X bond, the higher the energy of the nonbonding orbital and the greater the barrier $E_{e,0}$. Because triplet repulsion in the transition state with a reaction center like O…H…O is close to zero, $E_{e,0}$ for the class of reactions ($RO_2^{\bullet}$ + Ar_iOH) exhibits a minimum value (40–46 kJ/mol).

(2) The triplet repulsion is responsible for a higher activation barrier in the reactions of carbon-centered radicals with phenols (the reaction $R^{\bullet}$ + Ar_iOH). For example, the energy of the PhO–CH$_3$ bond is 270 kJ/mol, whereas the energy of the O–O bond in the hypothetical compound PhO–OOR is close to zero. As a result, the triplet repulsion increases $E_{e,0}$ from 43 kJ/mol in the reactions of $RO_2^{\bullet}$ with Ar_iOH to 61 kJ/mol in the reactions $R^{\bullet}$ + Ar_iOH.

(3) An increase in $E_{e,0}$ from 43 kJ/mol for the reaction $RO_2^{\bullet}$ + Ar_iOH to 51 kJ/mol for the reaction $RS^{\bullet}$ + Ar_iOH in the case of the reactions of phenols with thiyl radicals is due to additional repulsion because of an increase in the radius of the atom bearing a free valence and attacking phenol (cf. $r_{S-H} = 1.34 \times 10^{-10}$ m and $r_{O-H} = 0.97 \times 10^{-10}$ m). The above factors also affect the total elongation of reacting bonds in the transition state. Previously [12], it was found that this elongation ($\Delta r^{\neq}$) is constant for each class of radical reactions. A comparison of $\Delta r^{\neq}_{ArO...X}$ for various classes of reactions demonstrated that it reached a minimum for reactions with the reaction center O…H…O, where triplet repulsion was minimal: $\Delta r^{\neq}_{ArO...OOR} = 0.420 \times 10^{-10}$ m. For the reactions of thiyl radicals with phenols, this distance was much longer because of the effect of the bulky sulfur atom: $\Delta r^{\neq}_{ArO...SR} = 0.518 \times 10^{-10}$ m. In the transition states of the reactions of alkyl radicals with phenols, this elongation was even greater because of triplet repulsion: $\Delta r^{\neq}_{ArO...R} = 0.594 \times 10^{-10}$ m.

REFERENCES

1. Denisov, E.T. and Afanas'ev, I.B., *Oxidation and Antioxidants in Organic Chemistry and Biology*, Boca Raton, FL: CRC, Taylor and Francis Group, 2005.

2. *Oxidative Stress: Oxidants and Antioxidants*, Sies, H., Ed., New York: Academic, 1991.

3. Burlakova, E.B., Krashakov, S.A., and Khrapova, N.G., *Khim. Fiz.*, 1995, vol. 14, no. 10, p. 151 [*Chem. Phys. Rep.* (Engl. Transl.), vol. 14, no. 10, p. 1657].

4. Burton, G.A. and Ingold, K.U., *Acc. Chem. Res.*, 1986, vol. 19, no. 7, p. 194.

5. *Flavonoids: Chemistry, Biochemistry and Applications*, Andersen, O.M. and Markham, K.R., Eds., Boca Raton, FL: CRC, 2006.

6. Jovanovic, S.V., Steenken, S., Simic, M.G., and Hara, Y., in *Flavonoids in Health and Disease*, Rice-Evans, C.A. and Packer, L., Eds., New York: Marcel Dekker, 1998, p. 137.

7. Denisov, E.T. and Denisova, T.G., *Handbook of Antioxidants: Bond Dissociation Energies, Rate Constants, Activation Energies and Enthalpies of Reactions*, Boca Raton, FL: CRC, 2000.

8. Denisov, E.T., Denisova, T.G., Trepalin, S.V., and Drozdova, T.I., *Database of Oxidation and Antioxidants in Organic Chemistry*, Boca Raton, FL: CRC, Taylor and Francis Group, 2005.

9. Denisova, T.G. and Denisov, E.T., *Izv. Akad. Nauk, Ser. Khim.*, 2009, no. 9, p. 1824.

10. Denisov, E.T., *Usp. Khim.*, 1997, vol. 66, no. 10, p. 953 [*Russ. Chem. Rev.* (Engl. Transl.), vol. 66, no. 10, p. 859].

11. Denisov, E., in *General Aspects of the Chemistry of Radicals*, Alfassi, Z.B., Ed., Chichester: Wiley, 1999, p. 79.

12. Denisov, E.T. and Shestakov, A.F., *Izv. Akad. Nauk, Ser. Khim.*, 2003, no. 2, p. 306.

13. Denisova, T.G. and Denisov, E.T., *Kinet. Katal.*, 2004, vol. 45, no. 6, p. 877 [*Kinet. Catal.* (Engl. Transl.), vol. 45, no. 6, p. 826].

14. Denisova, T.G. and Denisov, E.T., *Neftekhimiya*, 2004, vol. 44, no. 4, p. 278 [*Pet. Chem.* (Engl. Transl.), vol. 44, no. 4, p. 250].

15. Denisov, E.T. and Tumanov, V.E., *Usp. Khim.*, 2005, vol. 74, no. 9, p. 905 [*Russ. Chem. Rev.* (Engl. Transl.), vol. 74, no. 9, p. 825].

16. Denisov, E., Cgatgiliologlu, C., Shestakov, A., and Denisova, T., *Int. J. Chem. Kinet.*, 2009, vol. 41, p. 284.

17. Evans, C., Scaiano, J.S., and Ingold, K.U., *J. Am. Chem. Soc.*, 1992, vol. 114, no. 12, p. 4589.

18. Franchi, P., Lucarini, M., Pedulli, G.F., Valgimigli, L., and Lunelli, B., *J. Am. Chem. Soc.*, 1999, vol. 121, no. 3, p. 507.

19. Lide, D.R., *Handbook of Chemistry and Physics*, Boca Raton, FL: CRC, 2004.

20. Barclay, L.R.C., Vinqvist, M.R., Mukai, K., Itoh, S., and Morimoto, H., *J. Org. Chem.*, 1993, vol. 58, no. 26, p. 7416.

21. Naumov, V.V. and Khrapova, N.G., *Biofizika*, 1985, vol. 30, no. 1, p. 5.

22. Pedrielli, P., Pedulli, G.F., and Skibsted, L.H., *J. Agric. Food Chem.*, 2001, vol. 49, no. 6, p. 3034.

23. Foti, M. and Ruberto, G., *J. Agric. Food Chem.*, 2001, vol. 49, no. 1, p. 342.

24. Belyakov, V.A., Roginsky, V.A., and Bors, W., *J. Chem. Soc., Perkin Trans. 2*, 1995, p. 2319.