The Chain-Breaking Antioxidant Activity of Phenolic Compounds with Different Numbers of O-H Groups as Determined During the Oxidation of Styrene

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ABSTRACT: The technique based on monitoring oxygen consumption was applied to test 18 polyphenols (PP) and model phenolics as a chain-breaking antioxidant during the oxidation of styrene initiated by 2,2′-azobis(2,4-dimethylvaleronitril) at 37°C. The chain-breaking capability of PP was characterized by two parameters: the rate constant k_1 for the reaction of antioxidants with the peroxy radical produced from styrene and the stoichiometric coefficient of inhibition, f, which shows how many kinetic chains are terminated by one molecule of PP. Rate constants $k_1 \times 10^5$ (in M^{-1} s^{-1}) were found to be 10 (catechol), 27 (pyrogallol), 34 (3,6-di-tert-Bu-catechol), 4.3 (protocatechic acid), 12 (gallic acid), 15 (caffeic acid), <0.01 (chrysin), 1.3 (kaempferol), 19 (quercetin), 5.3 (baicalein), 16 (epicatechin), 32 (epigallocatechin), 9.0 (dihydroquercetin), 3.3 (resveratrol), and 16 (nordihydroguaiaretic acid). The value of k_1 increases when going from one to two and three adjacent O-H groups in a benzene ring (catechol and pyrogallol derivatives, respectively). At the same time, two O-H groups in metaposition in a A-ring of flavonoids actually do not participate in the inhibition. For the majority of PP, f is near to 2 independent of the number of OH groups. The correlation of k_1 with the structure of PP and the O—H bond dissociation enthalpy has been discussed. © 2008 Wiley Periodicals, Inc. Int J Chem Kinet 41: 92–100, 2009

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INTRODUCTION

Polyphenols (PP), i.e., molecules having several hydroxyl groups on aromatic rings, are common constituents of foods of plant origin and are among major antioxidants of our diet. The main dietary sources of polyphenols are fruits and beverages such as tea, red wine, cacao, and coffee. The beneficial health effects of fruits and above-mentioned beverages against aging, cancer, and cardiovascular diseases are associated basically with PP antioxidant activity, i.e., with the capability of the PP of deactivating active free radicals [1–4]. It is generally agreed that the most principle reaction is that of PP (QH_2) with the peroxy radicals $LO_2^{\bullet}$

$$LO_2^{\bullet} + QH_2 \rightarrow LOOH + QH^{\bullet} \quad k_1 \qquad (1)$$

Reaction (1) is basically responsible for the antioxidant activity of PP. The antioxidant activity of PP, first of all flavonoids, has been the objective of numerous studies [5–10]. However, the majority of these studies are conducted by using indirect methods and the information reported is only of a qualitative or semiquantitative in nature.

The most adequate characteristic of the antioxidant activity is the rate constant k_1. Only for a few PP, reliable values of k_1 have been reported in the literature. The most justified approach to k_1 determination is that based on the application of the kinetic model of controlled chain oxidation. The key point of this approach is a constant and controlled rate of the initiation (active free radical generation). The latter is achieved, as a rule, by the application of thermolabile azo-compounds. The antioxidant activity of the chain-breaking antioxidants may be characterized by two independent parameters, k_1 and f, the stoichiometric coefficient of inhibition, which shows how many kinetic chains can be terminated by one molecule of antioxidant. The theoretically justified procedure for the determination of k_1 and f has been developed originally for monophenols [11–13], and then it was modified for PP by the examples of p-hydroquinones [14] and natural PP [15]. In this work, the subject for study was the antioxidant activity of the derivatives of catechol and pyrogallol during the oxidation of styrene. Styrene seems to be the best substrate for determining k_1. Along with other things, in this case reaction (1) is not complicated by a specific interaction of PP with a solvent and the value of k_1 determined may be considered as a genuine measure of the antioxidant reactivity. The structures of the antioxidants studied in this work are presented in Scheme 1.

MATERIALS AND METHODS

The commercial-grade sample of styrene was purged from antioxidants by using an alumina adsorption column with the subsequent distillation. A free radical initiator, 2,2′-azobis(2,4-dimethylvaleronitrile) (AMVN) was purchased from Polysciences Inc. Catechol, gallic acid, caffeic acid, epicatechin, and nordihydroguiaretic acid were purchased from Aldrich, and pyrogallol, 4-hydroxybenzoic acid, p-cumaric acid, chrysin, baicalein, resveratrol were obtained from Sigma. Kaempferol was purchased from Fluka, quercetin and dihydroquercetin from Serva, and myricetin and epigallocatecgin from Carl Roth. 3,6-di-tert-Bu-catechol was a gift from A. Wasserman. Other reagents used were of the highest available quality. Antioxidants were added to the testing system as a stock solution in chlorobenzene or in a mixture of acetonitrile with chlorobenzene, depending on the solubility.

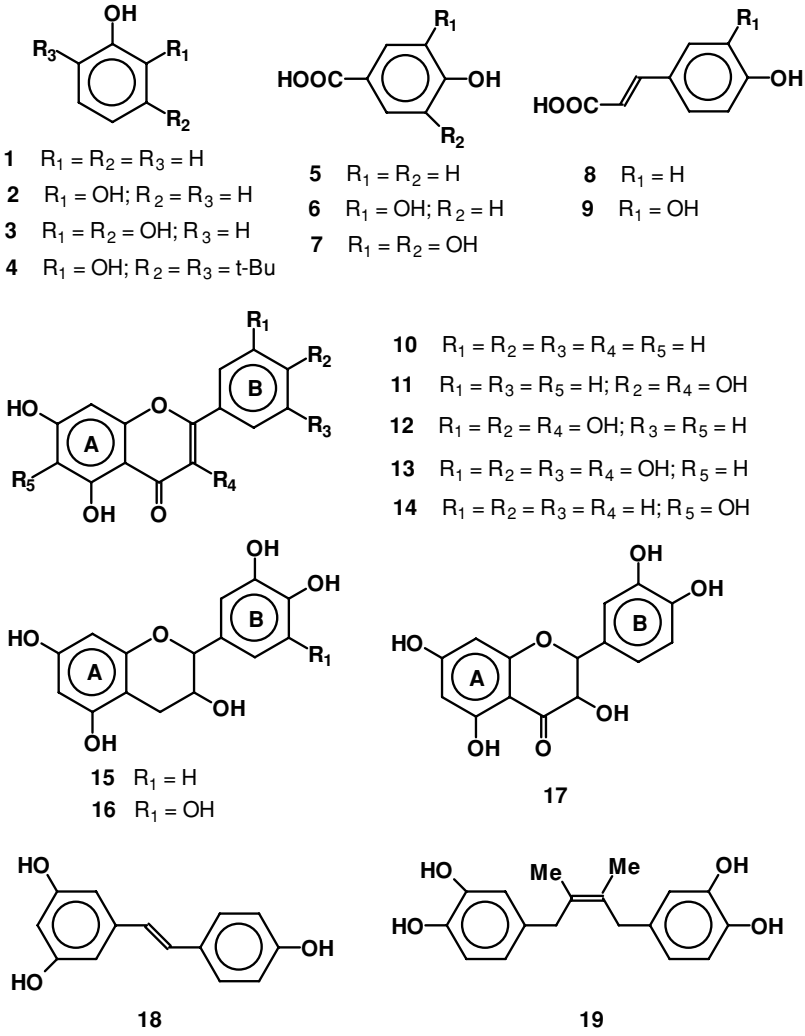
The kinetics of oxygen consumption during styrene oxidation initiated by AMVN was studied with a glass capillary microvolumometer of high sensitivity with a cell construction that allowed addition of required components without opening the cell [14]. All the runs were conducted at $37.0 \pm 0.1^{\circ}$C under air. The volume of the reaction mixture varied within the range from 0.5 to 1 mL. A kinetic run was started with measuring the rate of the oxidation in the absence of antioxidants, R_0, and the rate of initiation, R_{IN}. R_{IN} was varied by alteration of [AMVN] and was determined by the inhibitor method with 6-hydroxy-2,2,5,7,8-pentamethylchromane (HPMC) as a reference inhibitor. R_{IN} was calculated from the induction period of inhibited oxidation, t_{IND}, using Eq. (1)

$$R_{IN} = 2 \cdot [HPMC]/t_{IND} \qquad (1)$$

RESULTS AND DISCUSSION

Choosing Solvents

The majority of PP shows a very poor solubility in nonpolar solvents including styrene and chlorobenzene. Therefore, polar solvents are usually applied to prepare PP stock solutions. This presented a considerable challenge to the experiments. The fact is that many polar solvents form H-bonds with PP that results in significant reduction of the PP activity in reaction (1) [13,16]. This is a reason why the rate constants k_1 for PP reported in the literature are usually underestimated [13]. In this work, it was shown that even a very small addition of DMSO, one of the best solvents for PP, to the reaction mixture significantly decreased



Scheme 1

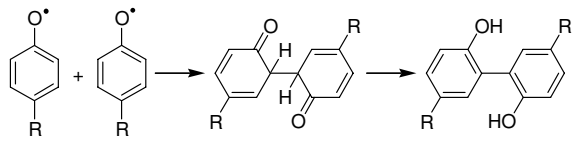
the experimental value of k_1 as compared with styrene or the styrene–chlorobenzene mixtures. For example, in the case of catechol (PP **2**) the addition of 0.012 M DMSO decreases k_1 by 2.5-fold, with caffeic acid (PP **9**), 0.0056 M DMSO caused a reduction of k_1 ca. 5-fold, with quercetin (PP **12**), with 0.014 M DMSO the k_1 was reduced by a factor of 3. To overcome this problem, DMSO in PP stock solutions was changed to acetonitrile (AN). Acetonitrile was reported to display a relatively moderate tendency to form H-bonds with phenolics and to reduce their reactivity [17]. In this work, the amount of AN in the reaction mixture never exceeded 0.5% (0.12 M). It was shown that such a concentration of AN did not reduce k_1 as compared to that measured in styrene.

Kinetic Scheme

The oxidation of styrene (LH) initiated by AMVN and inhibited by PP may be described by the classic kinetic Scheme 2 [12,13] slightly modified for the case, when a chain-breaking antioxidant is a hydroquinone (QH_2) [14]. Scheme 2 is presented for a "standard" peroxidation of substrate LH when hydroperoxide is a principle product that was formed by reaction (2) (for instance, polyunsaturated lipid). Meanwhile, during the oxidation of styrene chain propagation occurs as the addition of the peroxy radical to the double bond of styrene, resulting finally in the formation of polyperoxide rather

(0) AMVN + (LH + O_2) → $LO_2^\bullet$ + products	R_{IN}
(2) $LO_2^\bullet$ + LH + (O_2) → LOOH + $LO_2^\bullet$	k_2
(3) $LO_2^\bullet$ + $LO_2^\bullet$ → products	k_3
(1) $LO_2^\bullet$ + QH_2 → LOOH + $QH^\bullet$	k_1
(4) $QH^\bullet$ + $LO_2^\bullet$ → LOOH + Q	k_4
(5) $QH^\bullet$ + $QH^\bullet$ → QH_2 + Q	k_5

Scheme 2 Oxidation of LH initiated by AMVN and inhibited by QH_2.



Scheme 3

than hydroperoxide. However, from point of view of formal kinetics, this does not matter as all the kinetic equations are the same for both cases.

Attention should be drawn to the fact that both reactions (4) and (5) in Scheme 2 are presented as the disproportionation. The reason for that is the O–H bond in hydroxyl-substituted phenoxyls is rather weak [17], which makes reactions (4) and (5) thermodynamically profitable. This is in contrast to the reactions with participation of the phenoxy radical PhO$^\bullet$ formed from a monophenol PhOH

$$\mathrm{PHO}^\bullet + \mathrm{LO}_2^\bullet \rightarrow \text{Quinolide peroxide} \qquad (4a)$$

$$\mathrm{PhO}^\bullet + \mathrm{PhO}^\bullet \rightarrow \text{Products} \qquad (5a)$$

While reaction (4a) occurs unambiguously as the recombination with formation of quinolide peroxides [18], reaction (5a) may occur by both the mechanism of recombination or disproportionation depending on the PhO$^\bullet$ structure [12]. The recombination is typical of PhO$^\bullet$ in which the p-position or at least one of o-positions in the benzene ring is not substituted. The recombination occurs originally with formation of ketodimers followed by the enolization [12], for instance (Scheme 3). It should be noted that a final product of this process, dimer, has active O-H groups that can participate again in the reaction with $\mathrm{LO}_2^\bullet$.

Calculation of k_1/k_2 and f from [O_2] Traces

The reactivity of QH_2 to $\mathrm{LO}_2^\bullet$ is determined from the competition between reactions (1) and (2), and it is originally given as the k_1/k_2 ratio. The calculation of k_1/k_2 can be performed by using Eqs. (2) and (3)

$$F_1 = \mathrm{In}\frac{1 + R/R_0}{1 - R/R_0} - \frac{R_0}{R} = \frac{k_1 R_0}{n k_2 [\mathrm{LH}]} t + \text{constant} \qquad (2)$$

$$F_2 = \frac{R_0}{R} - \frac{R}{R_0} = \frac{2k_1 R_0}{n k_2 [\mathrm{LH}] R_{\mathrm{IN}}} [\mathrm{QH_2}] \qquad (3)$$

where R and R_0 are the rates of inhibited and noninhibited oxidation, respectively; [QH_2] is the starting concentration of QH_2; [LH] is the concentration of styrene (it is commonly very high and remains almost constant during a kinetic run). The deduction of Eqs. (2) and (3) has been reported elsewhere [14,19]. The coefficient n in the denominator of Eqs. (2) and (3) (1 or 2) depends on the fate of QH$^\bullet$. If QH$^\bullet$ terminates in reaction (4), $n = 1$; when reaction (5) predominates, $n = 2$. Equation (2) allows the calculation of k_1/k_2 directly from [O_2] trace. This way is suitable for rather reactive QH_2 when the concentration of QH_2 decreases significantly with time during a kinetic run (the "dynamic" method). It should be noted that the application of Eq. (2) does not require the use of R_{IN} and absolute concentration of QH_2. If the reactivity of QH_2 is relatively low and its concentration does not change significantly during a kinetic run, k_1/k_2 can be determined from the plot of the starting value of R vs. [QH_2] by using Eq. (3) (the "static" method). Equation (1) can be applied to determine the f value for QH_2, if [HPMC] is changed for [QH_2] and the coefficient 2 is changed for the variable f value

$$f = R_{\mathrm{IN}} \cdot t_{\mathrm{IND}} / [\mathrm{QH_2}] \qquad (4)$$

The determination of t_{IND} presents some difficulties. The "graphical" procedure commonly employed to determine t_{IND} from experimental [O_2] traces has no theoretical basis and is generally incorrect [14,15]. To circumvent these difficulties, it has been suggested to determine t_{IND} as the integral [14,15]

$$t_{\mathrm{IND}} = \int_{\infty}^{0} \left\{1 - (R/R_0)^2\right\} \, \mathrm{d}t \qquad (5)$$

Only this procedure was applied in this work.

Kinetic Parameters Characterizing the Chain-Breaking Capability of PP and Some Monophenols

The examples of kinetic runs aimed at determination of k_1/k_2 are depicted in Fig. 1 (the dynamic method) and Fig. 2 (the static method). As seen from Fig. 1, the plot of F_1 vs. time is a straight line as it is predicted by Eq. (2). The plot of F_2 vs. QH_2 concentration is also a straight line (Fig. 2) in accordance with Eq. (3). The value of k_1/k_2 can be calculated from the slope of these lines by using Eq. (2) or (3), respectively. In both cases, the absolute value of k_1 can be calculated from k_1/k_2, assuming that k_2 is equal to 57 $\mathrm{M^{-1}\ s^{-1}}$ [20]. The values of k_1 determined in this work are listed in Table I. In all the cases, the coefficient n in Eq. (2) or (3) was assumed to be equal to 2 (see below).

In Table I, stoichiometric coefficients f calculated for the more reactive antioxidants by using Eqs. (5) and (4) are also presented. As for the less active

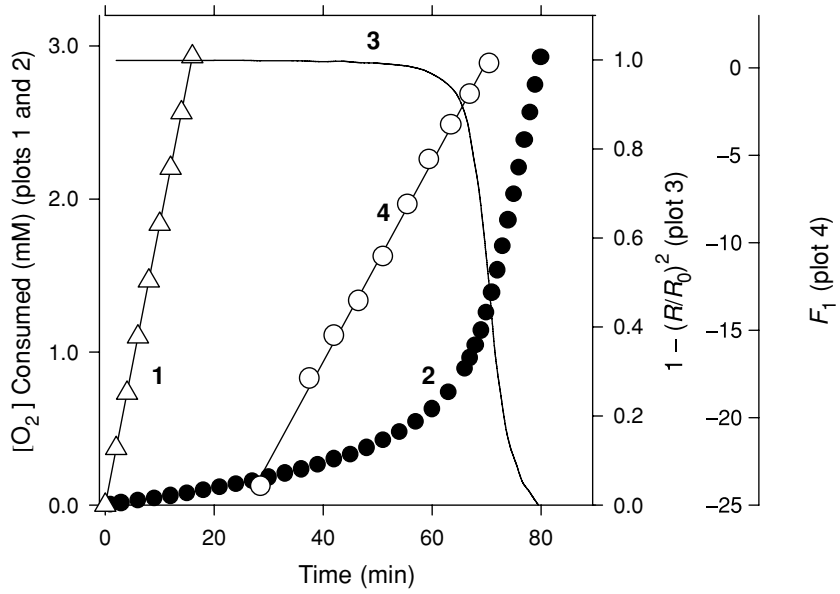


Figure 1 Kinetics of the oxidation of 8.5 M styrene at 37°C at $R_{IN} = 4 \times 10^{-9}$ M s^{-1}. Plot 1: [O_2] trace for the noninhibited oxidation; plot 2: [O_2] trace for the oxidation inhibited by 1×10^{-5} M pyrogallol (PP **3**); plot 3: trace 2 in the axes of Eq. (2); plot 3: the change of the parameter $1 - (R/R_0)^2$ with time; plot 4: trace 2 in the axes of Eq. (2).

antioxidants studied by the static method, experimental determination of f was evidently impossible in the framework of the technique applied. As Table I suggests, f is close to 2 for the majority of antioxidants studied including flavonoids containing several O-H groups, for instance **12**, **13**, **15**, and **17**. This value is also typical of numerous monophenols [12,13,21]. It is indicative that f for PP **19**, which contains two catechol moieties, is close to 4 (Table I), i.e., 2 for one catechol fragment. At the same time, for a few PP, first

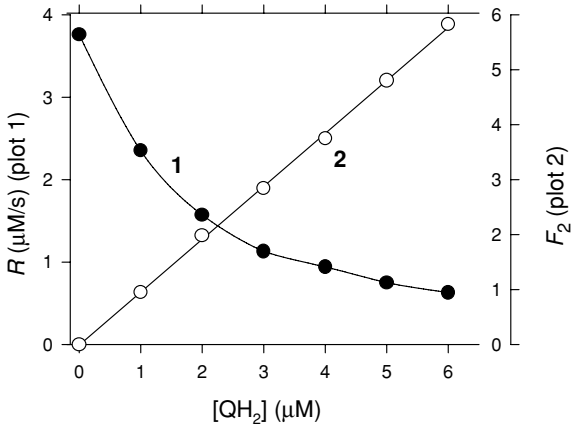


Figure 2 Kinetics of the oxidation of 8.5 M styrene at 37°C inhibited by *p*-cumaric acid (PP **8**) at $R_{IN} = 4 \times 10^{-9}$ M s^{-1}. Plot 1: Plot of the rate of oxidation against [QH_2]; plot 2: plot 1 in the axes of Eq. (3).

of all **6** and **7**, the f value is distinctly lower than two. Earlier this was reported for several *p*-hydroquinones, and this phenomenon was explained by the reaction of the *p*-hydroxy-substituted phenoxy radicals with molecular oxygen [14]. Experimentally, this manifests itself as a significant decrease in f, when R_{IN} is reduced [14]. This effect was not observed with the PP studied in this work (not shown). Starting from these observations, we can conclude that the contribution of the reaction of $QH^{\bullet}$ with O_2 is very moderate if any. So the reason for rather low values of f for **6**, **7** and some other PP remains unclear. Interestingly, the f value for some PP (**2**, **12**, **15**) determined during the oxidation of methyl linoleate in an aqueous micellar solution significantly exceeds 2 [15]. The difference in f determined in [15] and in the current work is likely caused by the difference in the nature of the antioxidant free radicals participating in the process under consideration. While in nonpolar styrene we deal with uncharged free radicals, in aqueous systems at neutral pH hydroxyl-substituted phenoxy radicals are deprotonated converting into a radical-anion.

Many PP, especially PP containing two or three adjusted OH groups, show a very high reactivity in reaction (1). k_1 for most active PP, **3**, **13**, **16**, which have in their structure three adjusted OH groups (Table I), is close to k_1 for α-tocopherol (3.3×10^6 M^{-1}s^{-1} [13,21]) known as the most active natural chain-breaking antioxidant.

Table I Kinetic Parameters Characterizing the Antioxidant Activity of PP and Model Antioxidants

Compound Number[a]	PP	Method	k_1 (M^{-1} s^{-1})[b]	f[b]
1	Phenol	–	$\sim 2 \times 10^3$[c]	–
2	Catechol	Dynamic	$(1.0 \pm 0.1) \times 10^6$	2.1 ± 0.2
3	Pyrogallol	Dynamic	$(2.7 \pm 0.2) \times 10^6$	1.8 ± 0.1
4	3,6-di-tert-Bu-catechol	Dynamic	$(3.4 \pm 0.3) \times 10^6$	2.0 ± 0.1
5	4-Hydroxybenzoic acid	Static	$(1.3 \pm 0.2) \times 10^3$	nd
6	Protocatechic acid	Dynamic	$(4.3 \pm 0.3) \times 10^5$	1.1 ± 0.1
7	Gallic acid	Dynamic	$(1.2 \pm 0.1) \times 10^6$	1.0 ± 0.1
8	*p*-Cumaric acid	Static	$(5.0 \pm 0.3) \times 10^4$	nd
9	Caffeic acid	Dynamic	$(1.5 \pm 0.1) \times 10^6$	1.5 ± 0.1
10	Chrysin	Static	$<10^3$[d]	nd
11	Kaempferol	Dynamic	$(1.3 \pm 0.1) \times 10^5$	>1.4
12	Quercetin	Dynamic	$(1.9 \pm 0.1) \times 10^6$	1.9 ± 0.1
13	Myricetin	Dynamic	$(2.8 \pm 0.2) \times 10^6$	1.6 ± 0.1
14	Baicalein	Dynamic	$(5.3 \pm 0.2) \times 10^5$	2.1 ± 0.1
15	Epicatechin	Dynamic	$(1.6 \pm 0.1) \times 10^6$	1.4 ± 0.1
16	Epigallocatechin	Dynamic	$(3.2 \pm 0.2) \times 10^6$	>0.9
17	Dihydroquercetin	Dynamic	$(9.0 \pm 0.5) \times 10^5$	1.9 ± 0.1
18	Resveratrol	Dynamic	$(3.3 \pm 0.2) \times 10^5$	2.1 ± 0.1
19	Nordihydroguaiaretic acid	Dynamic	$(1.6 \pm 0.1) \times 10^6$	4.1 ± 0.2

nd: Not determined.
[a] See Scheme 1.
[b] Averaged from at least four independent experiments.
[c] Reported in [20].
[d] No inhibition even at 0.2 mM chrysin.

For several PP studied in this work, k_1 was earlier reported in the literature. We shall restrict our consideration to the data obtained during the oxidation in nonpolar media. The values of k_1 during the oxidation of styrene were reported to be of 5.5×10^5 and 1.5×10^6 M^{-1} s^{-1} for catechols **2** and **4**, respectively [22], which are almost equal to k_1 determined in this work (if these are corrected for $n = 2$). The values of k_1 reported in [23] for **6** (6.5×10^4 $M^{-1}s^{-1}$) and for **9** (2.9×10^5 $M^{-1}s^{-1}$) are several fold lower than k_1 determined in this work (Table I). Most likely, the reason is that in work [23] the reaction mixture contained 0.1 M methanol that forms H-bonds with phenolics. Several k_1 values were determined during the oxidation of methyl linoleate (ML) [16,19]. All of them were also distinctly lower than these determined in the current work. Most likely, the effect is due to the occurrence of H-bond between QH_2 and the carboxy group of ML. If this is the case, the effect should become more pronounced when the ML concentration increases. The latter is in line with the experimental data. When the concentration of ML in the reaction mixture was only 0.24 M, the effect was rather moderate: with PP **12** and PP **15** k_1 was ca. 8×10^5 $M^{-1}s^{-1}$ (corrected for $n = 2$) [16] that is only twice as less as compared to k_1 measured in our work. When the reaction mixture consisted of nearly 100% ML [19], the effective values of k_1 were much lower: ca. 3×10^4 $M^{-1}s^{-1}$ for **9** and **12** (less than k_1 in Table I by nearly two orders of magnitude). A similar effect was also reported with several synthetic monophenols [24]. In a more general form, the reducing influence of H-bonds on reactivity of phenol antioxidants has been considered in other works [16,25].

With some PP studied in this work, very high k_1 values were reported during the oxidation of diphenylmethane (for instance, 1.5×10^7 M^{-1} s^{-1} for **9**, 2.1×10^7 $M^{-1}s^{-1}$ for **11**, 1.0×10^6 $M^{-1}s^{-1}$ for **10**) [26]. These values are higher than k_1 presented in Table I by nearly one order of magnitude. The difference in k_1 values between those reported by [26] and those determined in our work may only partly explain the elevated reactivity of $LO_2^{\bullet}$ from diphenylmethane [26]. One more reason for this difference could be the fact that in [26] determinations were conducted at the rate of initiation of 1.0×10^{-10} Ms^{-1} that is lower than typical values of R_{IN} in our work by one–two orders of magnitude. To rule out this reasoning, the determination of k_1 for catechol **2** was also performed at $R_{IN} = 4.0 \times 10^{-10}$ Ms^{-1} instead of 4.0×10^{-9} Ms^{-1}. In this case, k_1 was found to be 0.9×10^6 $M^{-1}s^{-1}$, which actually does not differ from that in Table I. In conclusion, the reason for so high values of k_1 in the work of [26] remains unclear.

Relationship of k_1 with the PP Structure

Let us consider how k_1 changes with the number and the position of OH groups. The following regularities may be noted:

1. Two meta-OH groups display a very low if any reactivity to $LO_2^{\bullet}$. For instance, chrysin that has no OH groups in ring B shows a very low reactivity, undetectable under our conditions. This is also evident from the fact that antioxidants containing two meta-OH groups along with other OH groups (flavonoids **11–13**, **15–17**, as well as resveratrol **18**) display f close to 2 (Table I). The latter means that meta-OH groups in the A-ring do not actually participate in the antioxidative action of the mentioned antioxidants. The low reactivity of meta-OH groups is also in line with the very moderate reduction in BDE as compared with the nonsubstituted phenol [27].
2. Antioxidants containing only one active OH group (**1, 5, 8, 10**) display a rather moderate reactivity to $LO_2^{\bullet}$, varying from 2×10^3 to 1.3×10^5 M^{-1} s^{-1}. Resveratrol **18** ($k_1 = 3.3 \times 10^5$ M^{-1} s^{-1} (Table I)) is a remarkable exception. There are numerous publications suggesting that resveratrol should show an outstanding chain-breaking antioxidant activity (see [28,29] and references therein). As a rule, the above speculations are based on indirect data. The k_1 value reported for **18** in this work has been determined directly for the first time. Despite a rather high value of k_1 for **18**, it is lower by nearly one order of magnitude than k_1 for many other natural PP, for instance **9**, **12**, **13**, **15**, and **16** (Table I).
3. k_1 increases dramatically up to (1–2) $\times 10^6$ M^{-1} s^{-1}, when going to the antioxidants containing two o-OH groups (catechol derivatives). This is evident when the following couples are confronted: **1** and **2**, **5** and **6**, **8** and **9**, and **11** and **12** (Table I). Meanwhile, the increase in the number of adjacent OH groups from two to three results in the subsequent increase in k_1 by a factor of 2–3 (compare **2** and **3**, **6** and **7**, **12** and **13**, and **15** and **16** (Table I)). Interestingly, baicalein **14**, a rather exotic flavonoid with three adjacent OH groups in the A-ring rather than in the B-ring (see Scheme 1) shows slightly lower reactivity as compared to myricetin **13**, pyrogallol **3** (also with three adjacent OH groups), and even in comparison with antioxidants with only two adjacent OH groups, **2**, **9**, **12**, and **15** (Table I).
4. As may be expected, the electron-withdrawing substituent —COOH causes the significant reduction of k_1 (compare **2** and **6**, **3**, and **7** in Table I). The occurrence of two bulky tert-butyl substituents in **4** results in the significant increase in k_1 as compared to the nonsubstituted catechol **2**.

Competition between Reactions (4) and (5). Coefficient n in Eqs. (2) and (3)

As mentioned above, the coefficient n depends on the predominant way of $QH^{\bullet}$ termination. The competition between reactions (4a) and (5a) has been considered for the case, when the antioxidant is a monophenol PhOH [12,29]. The contribution of reaction (4a), α, is given by the following relation:

$$\alpha^2(1+\alpha) - \frac{k_4^2 R_{IN}}{k_1^2 k_5 [PhOH]^2}(1-\alpha) = 0 \qquad (6)$$

Equation (6) still works with the change of [PhOH] for [QH_2]. The competition depends on five independent values, R_{IN}, [QH_2] ([PhOH]), k_1, k_4, and k_5. Whereas two first values are always known and k_1 is determined in the course of every run, the information on k_4 and k_5 for PP is highly limited (for PhOH $k_4 \approx 3 \times 10^8$ M^{-1} s^{-1} and actually independent of the PhOH structure [12]). As for k_4 for QH_2, this has never been reported. The values of k_5 reported in the literature for several PP fall within the range between 10^6 and 10^9 M^{-1} s^{-1} [12,30,31]. The estimations of the α value by using Eq. (6) show that the situation when $\alpha \ll 1$ (reaction (5) prevails over reaction (4)) is real in many cases, especially with the most active PP. For example, with the following reasonable combination of parameters: $k_1 = 1 \times 10^6$ M^{-1} s^{-1}; $k_4 = k_5 = 1 \times 10^8$ M^{-1} s^{-1}; $R_{IN} = 3 \times 10^{-9}$ Ms^{-1}; [QH_2] $= 1 \times 10^{-5}$ M, α was found to be 0.032. We may speculate that the situation, when reaction (5) predominates, is more typical. This is the reason why the coefficient n in Eqs. (2) and (3) applied to the calculation of k_1 listed in Table I is equal to 2. However, in the general case, the coefficient n can vary within the range from 1 to 2. It means that the values of k_1 in Table I are given with the uncertainty within the range (1–0.5)k_1.

Correlation of k_1 with the O—H Bond Dissociation Enthalpy

Bond dissociation enthalpy (BDE) for O—H bonds is one of the most significant factor in determining the reactivity of phenolics to $LO_2^{\bullet}$. So it is very promising to correlate k_1 with BDE. In contrast with monophenols

[12,32,33], the experimental information on BDE for O─H bonds in PP is highly limited [27,35]. It could be possible to make an attempt to correlate k_1 for PP with BDE calculated by using quantum-chemical methods, since extensive studies of such a kind have been published recently [27,36–41]. Unfortunately, the BDE values calculated for PP vary over rather a wide range when going from one work to another. For instance, the reported calculated values of BDE for catechol were (in kcal/mol): 72.8 [38], 74.7 [27], and 77.9 [41], which are visibly less than the experimental value of 80.5 [35]. Under these circumstances, we are forced to restrict our consideration to a general tendency. As calculations suggest, BDE decreases when the number of adjusted O─H groups increases from one to three. For instance, the work [27] reported the following values of BDE (in kcal/mol): 88 for phenol, ∼77 for PP with catechol moiety, and 72 for pyrogallol derivatives (the latter value belongs to the middle OH group [27]). At the same time, phenolics with two O─H groups in the metaposition (resorcinol derivatives) show a very small if any decrease in BDE as compared to phenol [42]. As for derivatives of gallic acid, the calculated value of BDE is significantly higher than in pyrogallols derivatives and is close to that in catechols [27]. The mentioned values of BDE are generally in line with the reactivity of PP as reported in Table I.

BIBLIOGRAPHY

1. Scalbert, A.; Manach, G.; Morand, C.; Remesy, C.; Jimenez, L. Crit Rev Food Sci Nutr 2006, 45, 287–306.
2. Manachi, C.; Donovan, J. L. Free Radical Res 2004, 38, 771–785.
3. Sang, S.; Hou, Z.; Lambert, J. D.; Yang, C. S. Antioxid Redox Signal 2005, 7, 1704–1714.
4. Lotito, S.; B.; Frei, B. Free Radical Biol Med 2006, 41, 1727–1746.
5. Rice-Evans, C.; Miller, N. J.; Paganga, G. Free Radical Biol Med 1996, 20, 933–956.
6. Roginsky, V.; Lissi, E. A. Food Chem 2005, 92, 235–254.
7. Heim, K. E.; Tagliaferro, A. K.; Bobilya, D. J. J Nutr Biochem 2002, 13, 572–584.
8. Silva, M. M.; Santos, M. R.; Caraco, G.; Rocha, R.; Justino, G.; Mira, L. Free Radical Res 2002, 36, 1219–1227.
9. Erlejman, A. G.; Verstraeten, S. V.; Fraga, C. G.; Oteiza, P. I. Free Radical Res 2004, 38, 1311–1320.
10. Burda, S.; Oleszek, W. J Agric Food Chem 2001, 49, 2774–2779.
11. Burton, G. W.; Doba, T.; Hughes, L.; Lee, E. L.; Ingold, K. U. J Am Chem Soc 1985, 107, 7053–7065.
12. Roginsky, V. A. Phenolic Antioxidants. Efficiency and Reactivity; Nauka: Moscow, 1988 (in Russian).
13. Barclay, L. R. C.; Vinqvist, M. R. In The Chemistry of Phenols; Rappoprt, Z. (Ed.); Wiley: New York, 2003; Part 2, Ch. 12.
14. Loshadkin, D.; Roginsky, V.; Pliss, E. 2002, Int J Chem Kinet 2002, 34, 162–171.
15. Roginsky, V. Arch Biochem Biophys 2003, 414, 261–270.
16. Pedrielli, P.; Pedulli, G. F.; Skibsted, L. H. J Agric Food Chem 2001, 49, 3034–3040.
17. Roginsky, V. A. J Org Chem 1989, 25, 403–413 (translated from Russian).
18. Roginsky, V. A.; Dubinsky, V. Z.; Shlyapnikova, I. A.; Miller, V. B. Eur Polym J 1977, 13, 1043–1051.
19. Roginsky, V. A.; Remorova, A. A.; Barsukova, T. K.; Bors, W. J Am Oil Chem Soc 1996, 73, 777–786.
20. Landolt-Börnstein Numerical Data and Relationships in Science and Technology New Series, Group II; Springer: Berlin, 1984; Vol. 13d.
21. Ross, A. B.; Mallard, W. G.; Helman, W. P.; Buxton, G. F.; Huie, R. E.; Nets, P. NDRL-NIST Solution Kinetics Datanase, Version 2; NST Standard Reference Data, Gaithersburg, MD, 1994.
22. Xi, P.; Barclay, R. C. Can J Chem 1998, 76, 171–182.
23. Amorati, R.; Pedulli, G. F.; Cabriani, L.; Zambonin, L.; Landi, L. J Agric Food Chem 2006, 54, 2932–2937.
24. Roginsky, V. A. Kinet Catal 1990, 31, 475–481 (translated from Russian).
25. Litwinenko, G.; Ingold, K. U. Acc Chem Res 2007, 40, 222–230.
26. Beljakov, V. A.; Roginsky, V. A.; Bors, W. J Chem Soc, Perkin Trans 1995, 2, 2319–2326.
27. Wright, J. S.; Johnson, E. R.; DiLabio, G. A. J Am Chem Soc 2001, 123, 1173–1183.
28. Hao, Y. D.; He, L. R. J Med Food 2004, 7, 290–298.
29. Fremont, L. Life Sci 2000, 66, 663–673.
30. Land, E. J Chem Soc, Faraday Trans 1993, 89, 803–810.
31. Deeble, D. J.; Parsons, B. J.; Philips, G. O.; Schuchmann, H.-P.; von Sonntag, C. Int J Radiat Chem 1988, 54, 179–193.
32. Mulder, P.; Saastad, O. W.; Griller, D. J Am Chem Soc 1988, 110, 4090–4092.
33. Jonsson, M.; Lind, J.; Eriksen, T. E.; Merenyi, G. J Chem Soc, Perkin Trans 1993, 2, 1567–1568.
34. Lucarini, M.; Mugnaini, V.; Pedulli, G. F. J Org Chem 2002, 67, 928–931.
35. Suryan, M. M.; Kafafi, S. A.; Stein, S. E. J Am Chem Soc 1989, 111, 4594–4600.
36. Giacomelli, C.; da Silva Miranda, F.; Gonçalves, N. S.; Spinelli, A. Redox Rep 2004, 9, 263–269.
37. Leopoldini, M.; Marino, T.; Russo, N.; Toscano, M. J Phys Chem A 2004, 108, 4916–4922.
38. Zhang, H.-Y.; Sun, Y.-M.; Wang, X.-L. Chem Eur J 2003, 9, 502–508.

39. Hussain, H. H.; Babic, G.; Durst, T.; Wright, J. S.; Flueraru, M.; Chichirau, A.; Chepelev, L. L. J Org Chem 2003, 68, 7023–7032.
40. Cren-Olive, C.; Hapiot, P.; Pinson, J.; Rolando, C. J Am Chem Soc 2002, 124, 14027–14038.
41. Nenadis, N.; Wang, L.-F.; Tsimidou, M. Z.; Zhang, H.-Y. J Agric Food Chem 2005, 53, 295–299.
42. Thavasi, V.; Leong, L. P.; Bettens, R. P. A. J Phys Chem A 2006, 110, 4918–4923.