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Antioxidant Properties of 2,4-Diphenyl-7,8-Benzo-5,6-Dihydro(4H)selenochromene and 2-*para*-Chlorophenyl-4-Phenyl-7,8-Benzo-5,6-Dihydro(4H)selenochromene

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Abstract—The antioxidant properties of 2,4-diphenyl-7,8-benzo-5,6-dihydro(4H)selenochromene and 2-*para*-chlorophenyl-4-phenyl-7,8-benzo-5,6-dihydro(4H)selenochromene were studied using the initiated oxidation of ethylbenzene and propan-2-ol as model reactions. The antioxidant activity of these compounds was quantitatively characterized by the apparent rate constant of inhibition, fk_{in}. Addition of 2,4-diphenyl-7,8-benzo-5,6-dihydro(4H)selenochromene to ethylbenzene being oxidized increases the chemiluminescence intensity.

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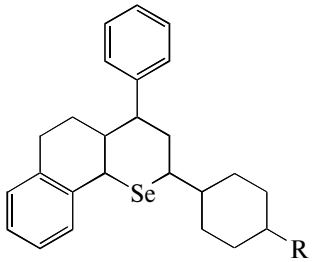
Selenium is a biologically active microelement. It is a component of a number of hormones and enzymes and is essential for the vital functions of the animals and man. The most significant biological function of selenium is ensuring the efficient work of the protective antioxidant system of the living organism [1–6]. Selenium is involved in the functioning of glutathione peroxidase, which decomposes hydrogen peroxide and lipoperoxides and thus prevents cellular membranes from oxidative destruction [5]. Synthetic organoselenium compounds also possess pronounced antioxidant properties [5]. However, information on their antioxidant activity is mainly semiquantitative, causing serious difficulties in the prediction of their reactivity as antioxidants under variable conditions.

Here, we report quantitative determination of the antioxidant effect of 2,4-diphenyl-7,8-benzo-5,6-dihydro(4H)selenochromene (**I**) and 2-*para*-chlorophenyl-4-phenyl-7,8-benzo-5,6-dihydro(4H)selenochromene (**II**) using the initiated oxidation of ethylbenzene and propan-2-ol as model reactions.

EXPERIMENTAL

Propan-2-ol and ethylbenzene were purified according to standard procedures [7, 8]. The initiator azobisisobutyronitrile (AIBN) was twice recrystallized from ethanol and dried in vacuo.

Antioxidants with the general structural formula



R = H (**I**) or Cl (**II**)

were synthesized according to a known procedure [9, 10] and were used without additional purification. Their characteristics were determined by elemental analysis and ^{1}H NMR spectroscopy.

Compound **I**: mp 108–109°C.

For $C_{25}H_{20}Se$ anal. calcd. (%): C, 75.18; H, 5.05. Found (%): C, 74.75; H, 5.27.

^{1}H NMR ($CDCl_3$), δ, ppm: 6.89–7.49 (m, 14H, H_{arom}), 6.30 (d, 1H, β-H, J = 5.8 Hz), 4.37 (d, 1H, γ-H, J = 5.8 Hz), 2.88–2.67 (m, 2H, CH_2), 2.38–2.19 (m, 2H, CH_2).

Compound **II**: mp 126–128°C.

For $C_{25}H_{19}SeCl$ anal. calcd. (%): C, 69.21; H, 4.41. Found (%): C, 69.03; H, 4.66.

^{1}H NMR ($CDCl_3$), δ, ppm: 7.05–7.49 (m, 13H, H_{arom}), 6.24 (d, 1H, β-H, J = 5.4 Hz), 4.34 (d, 1H, γ-H, J = 5.9 Hz), 2.86–2.49 (m, 2H, CH_2), 2.35–1.97 (m, 2H, CH_2).

The antioxidant activity of the selenochromene derivatives was estimated as the rate of oxygen uptake

from air by the substrates being oxidized (ethylbenzene and propan-2-ol) at 336–363 K (AIBN as the initiator, initiation rate of $w_i = 1 \times 10^{-7}$ mol l^{-1} s^{-1}), using a manometric setup detailed in [11]. Chemiluminescence measurements in the visible spectral region (S-11 photomultiplier) were also performed.

Oxidation was carried out in a temperature-controlled glass reactor fitted with a reflux condenser. Solutions of the initiator and antioxidants in the model substrates were placed into the reactor. The intensity of the chemiluminescence signal was displayed using a chart recorder. The inhibition effect of the selenochromene derivatives was estimated as the decrease of the initial oxygen uptake rate, whose numerical value was derived from 5 to 8 points in the initial portion of the oxygen uptake curve using the least-squares method.

The initiation rate was calculated as $w_i = k_i$[AIBN], where k_i is the initiation rate constant. It was accepted in the calculation that $k_i = 2ek_p$, where k_p is the rate constant of AIBN decomposition and e is the probability of a radical escaping to the bulk [12, 13]. The rate constant of AIBN decomposition in the ethylbenzene medium was calculated using the equation

$$\log k_p = 15.42 - 31.2/(4.575T \times 10^{-3}),$$

accepting that $e = 0.5$ [12]. The k_p value for the propan-2-ol medium was taken to be equal to the rate constant of AIBN decomposition in cyclohexanol:

$$\log k_p = 17.70 - 35/(4.575T \times 10^{-3})$$

with $e = 0.5$ [12].

The antioxidant activity of the selenochromene derivatives was characterized by the apparent inhibition rate constant fk_{in}, where f is the radical capacity of the antioxidant, which is the number of radical intermediates decaying on one antioxidant molecule in chain termination events [13].

RESULTS AND DISCUSSION

The antioxidant activity of the two selenochromene derivatives was studied using the initiated oxidation of propan-2-ol and ethylbenzene as model reactions. Under standard experimental conditions, the initiated oxidation of the model substrates was kinetically controlled and occurred via a radical chain mechanism with quadratic-law chain termination. It included a number of elementary steps common for most organic compounds[1] [5, 12, 13]:

$$\text{(i) } I \rightarrow 2r^{\bullet},\ r^{\bullet} + O_2 \rightarrow rO_2^{\bullet}\ rO_2^{\bullet} + RH \rightarrow rO_2H + R^{\bullet},$$

$$\text{(1) } R^{\bullet} + O_2 \rightarrow RO_2^{\bullet},$$

[1] Elementary step numbering conventional for the oxidation mechanism is used here.

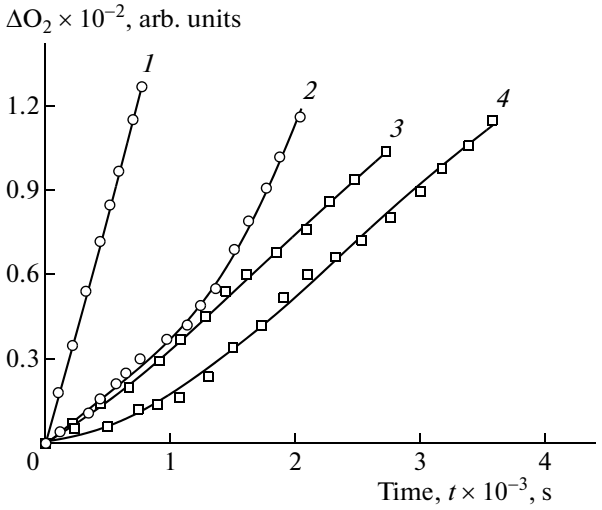


Fig. 1. Typical oxygen uptake kinetics ($T = 348$ K, $w_i = 1 \times 10^{-7}$ mol l^{-1} s^{-1}) in EB oxidation (*1*) in the absence of AO and (*2–4*) in the presence of selenochromene derivatives: (*2*) [**I**] $= 1.25 \times 10^{-4}$, (*3*) [**II**] $= 1.8 \times 10^{-4}$, and (*4*) [**II**] $= 3.25 \times 10^{-4}$ mol/l.

$$\text{(2) } RO_2^{\bullet} + RH \rightarrow ROOH + R^{\bullet},$$

.....

$$\text{(6) } 2RO_2^{\bullet} \rightarrow RH_2OH + R'CHO,$$

$$\text{(7) } RO_2^{\bullet} + InH \rightarrow ROOH + In^{\bullet},$$

$$\text{(8) } RO_2^{\bullet} + In^{\bullet} \rightarrow \text{molecular products},$$

where $R^{\bullet}$ and $RO_2^{\bullet}$ are the alkyl and peroxyl radicals of ethylbenzene or the oxyalkyl and hydroperoxyl radicals of propan-2-ol $(Me)_2C(OH)OO^{\bullet}$, respectively, and $R' = C_6H_5$ (for ethylbenzene as the model substrate).

The introduction of an antioxidant (AO) into the model system was expected to decrease the rate of substrate oxidation owing to chain termination on molecules of the inhibiting admixture (step 7) [5], and this was actually observed in the experiment (Fig. 1).

It should be taken into account that ethylbenzene and propan-2-ol are oxidized via different mechanisms. According to the literature [14], propan-2-ol is oxidized by the hydroperoxyl radicals resulting from the decomposition of the primary oxyperoxyl radicals $(Me)_2C(OH)OO^{\bullet}$ (step 2a). Therefore, the oxidation chain termination under long chain retention conditions also occurs on $HO_2^{\bullet}$ radicals:

$$\text{(2a) } (Me)_2C(OH)OO^{\bullet} \rightarrow (Me)_2C{=}O + HO_2^{\bullet},$$

$$\text{(2b) } HO_2^{\bullet} + RH \rightarrow H_2O_2 + R^{\bullet},$$

.....

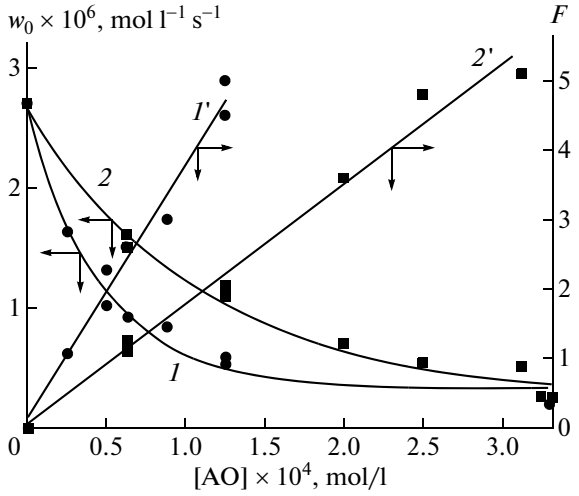


Fig. 2. Dependences of the (*1*, *2*) ethylbenzene oxidation rate and (*1'*, *2'*) parameter *F* on the initial concentration of (*1*, *1'*) **I** and (*2*, *2'*) **II**. Correlation coefficients: (*1'*) $r = 0.98$; (*2'*) $r = 0.97$. $T = 348$ K, $w_i = 1 \times 10^{-7}$ mol l^{-1} s^{-1}.

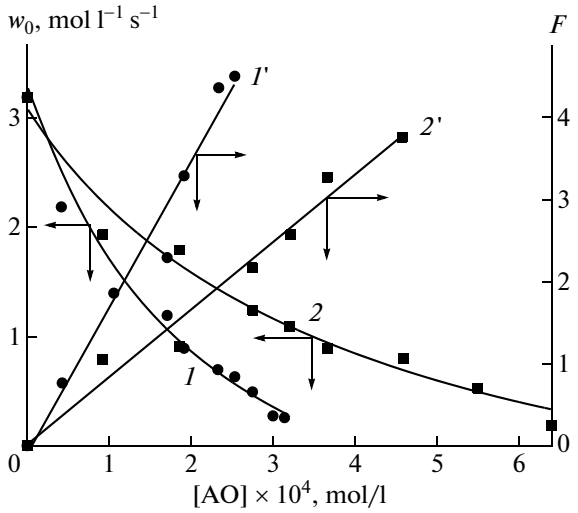


Fig. 3. Dependences of the (*1*, *2*) propan-2-ol oxidation rate and (*1'*, *2'*) parameter *F* on the initial concentration of (*1*, *1'*) **I** and (*2*, *2'*) **II**. Correlation coefficients: (*1'*) $r = 098$; (*2'*) $r = 0.99$. $T = 348$ K, $w_i = 1 \times 10^{-7}$ mol l^{-1} s^{-1}.

$$\text{(6a)}\ 2HO_2^{\bullet} \rightarrow H_2O_2 + O_2,$$

$$\text{(7a)}\ HO_2^{\bullet} + InH \rightarrow H_2O_2 + In^{\bullet},$$

$$\text{(8a)}\ HO_2^{\bullet} + In^{\bullet} \rightarrow InH + O_2.$$

Addition of the selenochromene derivatives to the substrates being oxidized decreases the initial oxygen uptake rate, indicating their antioxidant effect. The dependences of the initial rate of oxidation of the model substrates on the concentration of **I** and **II** are shown in Figs. 2 and 3.

To determine fk_{in}, the experimental results were represented in the coordinates of Eqs. (1) and (2) [13, 14]:

$$F = \frac{w_0^0}{w_0} - \frac{w_0}{w_0^0} = fk_{in}[AO]/\sqrt{2k_6 w_i}, \qquad (1)$$

where [AO] is the inhibitor concentration; w_0^0 and w_0 are the initial oxygen uptake rates in the absence and presence of the inhibitor, respectively; $2k_6 = 1.91 \times 10^7$ l mol^{-1} s^{-1} for ethylbenzene [12]; and $2k_6 = 3.45 \times 10^7$ l mol^{-1} s^{-1} for propan-2-ol [14].

Apparent inhibition rate constants calculated using Eqs. (1) and (2)

Antioxidant	Substrate	fk_{in}, l mol^{-1} s^{-1}	
		Eq. (1)	Eq. (2)
I	EB	5.3 ± 0.5	2.6 ± 1.0
II		3.6 ± 0.5	2.0 ± 0.1
I	Propan-2-ol	3.0 ± 0.5	–
II		1.7 ± 0.3	–

The dependences of the ethylbenzene (EB) oxidation rate on the concentrations of introduced selenochromenes tend to a limit (Fig. 2): when the concentrations [**I**] = 1.25×10^{-4} mol/l and [**II**] = 3.32×10^{-4} mol/l are reached, the rate of ethylbenzene oxidation stops depending on the concentration of these compounds. The oxidation chain is terminated mainly on antioxidant molecules via the linear-law mechanism, which is indicated by the fulfillment of Eq. (2) (correlation coefficient of $r = 0.98$; Fig. 3)

$$w_0 = \frac{k_2[EB]}{fk_{in}[AO]} w_i, \qquad (2)$$

where k_2 is the rate constant of ethylbenzene chain propagation, which is 3.8 l mol^{-1} s^{-1} [5, 12], and [EB] = 8.17 mol/l.

Based on these data, we calculated the apparent inhibition rate constants fk_{in} for the selenochromene derivatives. The calculated data are listed in the table. Thus, the experimental data obtained by two different kinetic methods are similar (Figs. 2, 4).

The oxidation of ethylbenzene is accompanied by chemiluminescence which is typical of the radical chain oxidation of many organic compounds. The introduction of antioxidants terminating the oxidation chain at the peroxyl radical step (step 7) usually results in the quenching of chemiluminescence [5, 6]. However, the presence of selenochromene concentrations causing a substantial decrease in the initial rate of ethylbenzene oxidation (Fig. 1) favors an increase in chemiluminescence intensity. To study the nature of the emission, we performed a series of experiments on ethylbenzene oxidation in the presence and absence of **I** and on chlorobenzene oxidation in the absence of AIBN. The results of these experiments are shown in

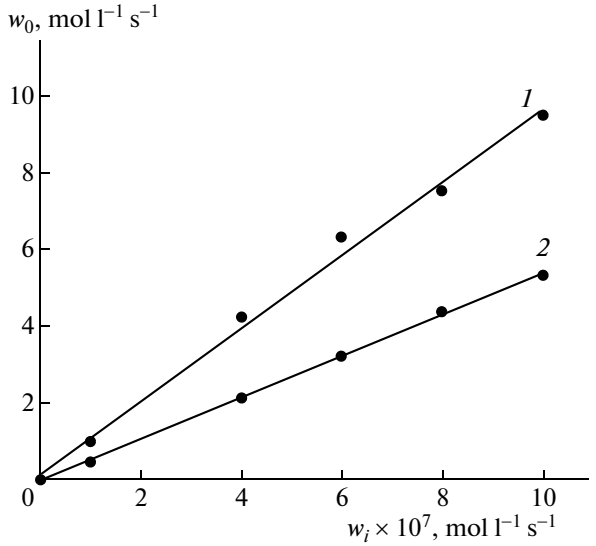


Fig. 4. Dependences of the rate of inhibited EB oxidation on the initiation rate in the presence of [**I**] = 1.25 × 10^{-4} mol/l and [**II**] = 3.32 × 10^{-4} mol/l; T = 348 K.

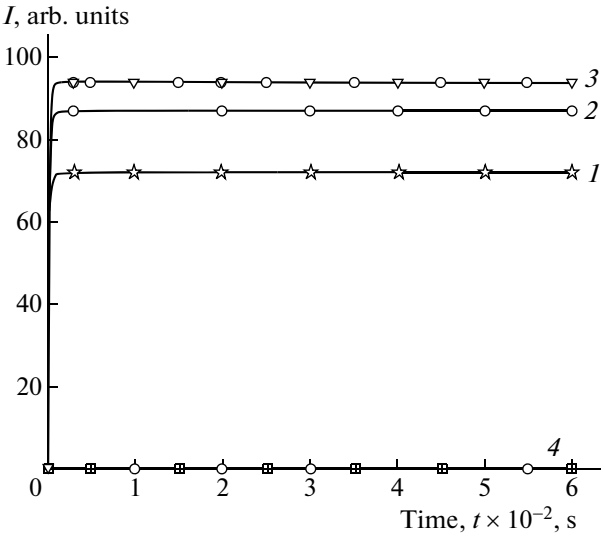


Fig. 5. Influence of **I** on the chemiluminescence intensity during the oxidation of EB and chlorobenzene (CB) with atmospheric oxygen: (*1*) EB + AIBN, (*2*) EB + AIBN + **I** ([**I**] = 1.23 × 10^{-5} mol/l), (*3*) EB + AIBN + **I** (▽, [**I**] = 7.3 × 10^{-5} mol/l; ●, [**I**] = 3.6 × 10^{-5} mol/l), and (*4*) CB + **I** (●, [**I**] = 3.6 × 10^{-5} mol/l; ⊞, [**I**] = 3 × 10^{-4} mol/l); T = 348 K; w_i = 1 × 10^{-7} mol l^{-1} s^{-1}.

Fig. 5. In the absence of an initiator, chlorobenzene oxidizes slowly and no emission is observed. The nature of the anomalous behavior of chemiluminescence in the presence of the selenochromenes will be the subject of forthcoming studies.

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