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REACTIONS OF DIPHENYL SELENIDE AND DIPHENYL SELENOXIDE  
WITH CUMENE HYDROPEROXIDE

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The reaction products of selected organoselenium compounds, diphenyl selenide and diphenyl selenoxide with model lipid hydroperoxide, cumene hydroperoxide, were studied using gas chromatography-mass spectrometry and high-performance liquid chromatography methods, as well as the release of free radicals was determined by the inhibitor method. It has been established, that the reaction products of the studied organoselenium compounds and cumene hydroperoxide are dimethylphenylcarbinol, acetophenone and  $\alpha$ -methylstyrene, and the reaction sequentially continues until the formation of diphenylselenone. It was also confirmed by the inhibitor method that these reactions proceed without the formation of free radicals.

Ref. 6, fig. 3, tabl. 1

**Keywords:** diphenyl selenide, diphenyl selenoxide, cumene hydroperoxide, antioxidant.

Introduction

In living organisms natural and synthetic organoselenium compounds exhibit antioxidant, anticancer, antimicrobial and antiviral properties [1-4]. They mainly act as two-electron reducing agents in reaction with toxic hydroperoxides, which are the main lipid oxidation products by dioxygen, converting them into relatively non-toxic alcohols. Synthetic selenic compounds (e.g. Ebselen, which is widely used as a selenium containing medical drug) structurally similar to the organoselenium compounds considered in the current article are analogs of the enzyme glutathione

peroxidase. They exhibit high bioactivity, haven't negative distinctive properties, that are mainly associated with the presence of other heteroatoms in the molecule (nitrogen, oxygen, etc.) and conjugated unsaturated chemical bonds [5]. However, detailed information on the chemical mechanisms of the antioxidant action of these organoselenium compounds is insufficient.

The study of the reactions of organoselenium antioxidants with organic hydroperoxides (reactive oxygen species formed during lipid oxidation) is considered relevant.

### Experimental

The organoselenium compound diphenyl selenoxide (DSeO) was synthesized by the method described in [6], and diphenyl selenide (DSe) was purchased from the chemical company Sigma-Aldrich (USA). Other chemicals: cumene hydroperoxide ( $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)_2\text{OOH}$ ),  $\alpha$ -methylstyrene ( $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$ ), dimethyl phenyl carbinol ( $(\text{CH}_3)_2\text{C}(\text{OH})\text{C}_6\text{H}_5$ ), acetophenone ( $\text{CH}_3\text{COC}_6\text{H}_5$ ),  $\beta$ -naphthylamine ( $\text{C}_{10}\text{H}_7\text{NH}_2$ ), solvent chlorobenzene were also purchased from the same company.

The reactions between organoselenium compounds (Fig. 1) with model lipid hydroperoxide, cumene hydroperoxide (CHP), as well as the reaction products' analysis were studied by gas chromatography system coupled with a mass spectrometry detector (GC-MS system CLARUS 680 GC-MS, Perkin Elmer, USA) and high performance liquid chromatography system coupled with UV spectrometry detector (LC 300 HPLC system, Perkin Elmer, USA). The GC-MS system was equipped with a Thermo TR-5MS fused silica capillary column ( $30\text{ m} \times 0.25\text{ mm}$ ) with  $0.25\text{ }\mu\text{m}$  film thickness of coated material. Helium was used as the carrier gas, with a flow rate of  $1\text{ ml/min}$  and a split flow of  $25\text{ ml/min}$ . The transfer line temperature was set at  $250^\circ\text{C}$ . In HPLC system C18 column ( $4.6\text{ mm} \times 250\text{ mm i.d.}, 5\text{ }\mu\text{m}$ ) was used for the separation and the mobile phase was consisted of water (A) and acetonitrile (B) and the flow rate was  $1\text{ ml/min}$ . The mobile phase was programmed consecutively in a linear gradient as follows:  $0\text{ min}$  (80% A);  $20\text{ min}$  (20% A). The multi-wavelength detector was monitored at 230 and  $254\text{ nm}$ , the injection volume was  $1\text{ }\mu\text{l}$  for each sample solution. The oven temperature was maintained at  $35^\circ\text{C}$ .

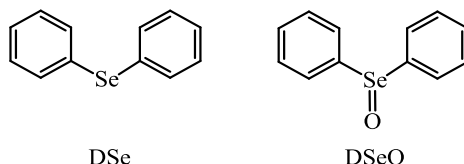


Fig. 1. Structural formulas of the diphenyl selenide and diphenyl selenoxide.

The experiments were carried out at  $T=37\pm0.1^{\circ}\text{C}$  temperature for 3 h. The studied antioxidants' and cumene hydroperoxide concentration were  $1.5\times10^{-2}\text{ mol/l}$ .

The release of free radicals in the reaction of the studied organoselenium compounds, DSe, DSeO with cumene hydroperoxide in the presence of  $\beta$ -naphthylamine (neozone-D) was determined by inhibitors' method using fluorescence spectrometer Perkin-Elmer MPF-44B (USA). The  $\beta$ -naphthylamine concentration was  $3\times10^{-6}\text{ mol/l}$ , and a change in signal intensity over time was recorded at 453 nm.

## Results and Discussion

The study of the reactions between DSe, DSeO and model lipid hydroperoxide, CHP, shows that the main product of the reactions mentioned above is dimethyl phenyl carbinol. Acetophenone (APh) and  $\alpha$ -methylstyrene are also formed, but in relatively smaller quantities.

It follows from the table that in the case of diphenylselenide, the consumption of cumene hydroperoxide is greater than in the case of diphenyl selenoxide.

The CHP consumption in relation with consumption of studied organoselenium compounds are given in Table 1.

**Table 1**

**CHP consumption in relation with consumption of DSe and DSeO compounds**

Se-Org	DSe	DSeO
$\frac{\Delta[\text{ROOH}]}{\Delta[\text{Se-Org}]}$	$0.8\pm0.1$	$1.9\pm0.05$

From the data given in Table 1 it follows, that in the case of DSe, the consumption of CHP is greater than in the case of DSeO, that is the reaction is sluggish.

The HPLC analysis results for reaction of DSeO with CHP are given in Fig. 2.

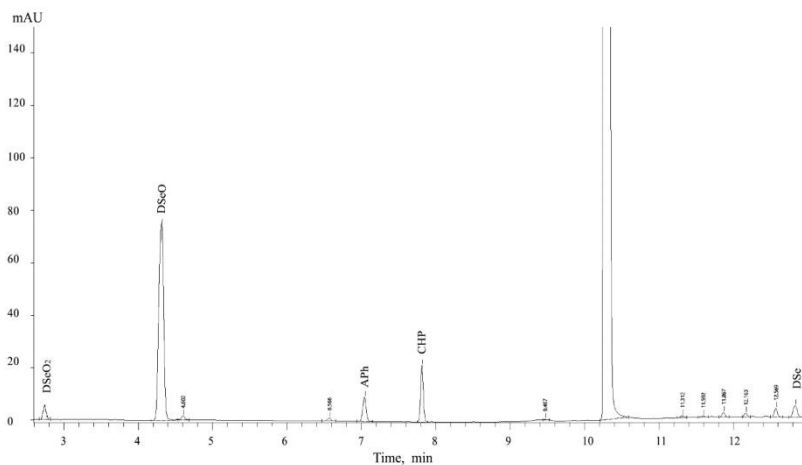


Fig. 2. HPLC chromatograms of reaction products of DSeO with CHP.

The detailed analysis of the given chromatogram shows, that along with the reaction products mentioned above, the diphenyl selenone (DSeO<sub>2</sub>) is also formed.

It is also clear from the obtained data that the signal intensity of  $\beta$ -naphthylamine (neozone-D) did not decrease, which means that in the reactions of the studied organoselenium compounds, DSe, DSeO with CHP no free radicals are formed (within the accuracy of the used method). The yield of radicals in the reaction is estimated as  $< 10^{-5}$ . The dominance of reactive radical-free conversion of hydroperoxide is an important characteristic of the antihydroperoxide activity of antioxidants.

Based on the results, the antihydroperoxide scheme of selected organoselenium compounds can be presented as follows:

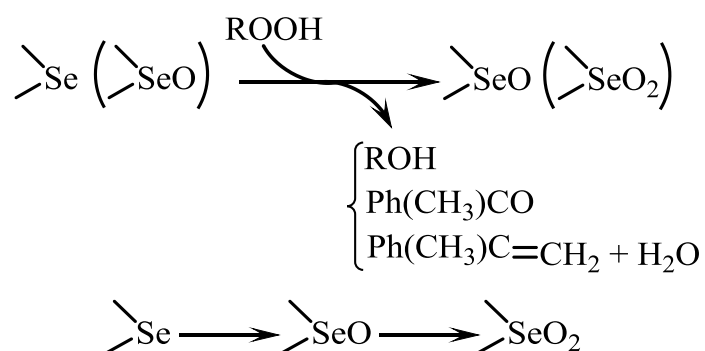


Fig. 3. Proposed scheme of chemical transformations of the antihydroperoxide action of selected organoselenium compounds.

## Conclusion

Thus, it can be concluded that the studied organoselenium compounds, have antihydroperoxide action in the reaction with CHP, turning them into relatively non-toxic stable products without detecting the formation of free radicals. The revealing of the mechanism of the antihydroperoxide action of organoselenium compounds will make it possible to predict new selenium-containing bioactive structures with a greater antioxidant potency, which will have high bioavailability and will be non-toxic to living organisms.

### ԴԻՖԵՆԻԼՍԵԼԵՆԻԴ և ԴԻՖԵՆԻԼՍԵԼԵՆՕՔՍԻԴԻ ԿՈՒՄՈԼԻ ՀԻԴՐՈՊԵՐՕՔՍԻԴԻ ՀԵՏ ՌԵԱԿՑԻԱՆԵՐԸ

Ա.Ղ. ՄԱՀԱԿՅԱՆ, Գ.Հ. ՔՈՉԱՐՅԱՆ, Լ.Ա. ԹԱՎԱԴՅԱՆ

*Գազ-հեղուկային - մաս սպեկտրաչափական և հեղուկային քրոմատոգրաֆիայի եղանակներով ուսումնասիրվել են դիֆենիլսելենիդի և դիֆենիլսելենօքսիդի մոդելային լիպիդային հիդրոպերօքսիդի՝ կոլմոլի հիդրոպերօքսիդի հետ ռեակցիաների արգասիքները, ինչպես նաև որոշվել է ռեակցիայում ազատ ռադիկալների ելքը՝ ինհիբիտորների եղանակով: Հաստատվել է, որ ուսումնասիրվող սելենօրգանական միացությունների և կոլմոլի հիդրոպերօքսիդի ռեակցիայի արգասիքներն են դիմեթիլ ֆենիլ կարբինոլը, ացետոֆենոնը և  $\alpha$ -մեթիլ ստիրոլը, իսկ ռեակցիան հաջորդաբար շարունակվում է մինչև դիֆենիլ սելենոնի առաջացում: Ինհիբիտորների եղանակով հաստատվել է նաև, որ նշված ռեակցիաներում ազատ ռադիկալներ չեն առաջանում:*

### РЕАКЦИИ ДИФЕНИЛ СЕЛЕНИДА И ДИФЕНИЛСЕЛЕНОКСИДА С ГИДРОПЕРОКСИДОМ КУМОЛА

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Исследованы продукты реакции избранных селенорганических соединений – дифенилселенида и дифенилселеноксида с модельным липидным гидропероксидом – гидропероксидом кумола методами газовой хромато-масс-спектрометрии и высокоэффективной жидкостной хроматографии, и также определен выход в реакции свободных радикалов методом ингибиторов. Установлено, что продуктами реакции изученных селенорганических соединений с гидропероксидом кумола являются диметилфенилкарбинол, ацетофенон и  $\alpha$ -метилстирол, при этом реакция последовательно продолжается до образования дифенилселенона. Также методом ингибиторов, установлено, что в указанные реакции протекают без образования свободных радикалов.

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