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CHEMISTRY

Study of the Antioxidant Properties of Phosphorylated Phenols

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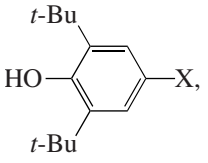
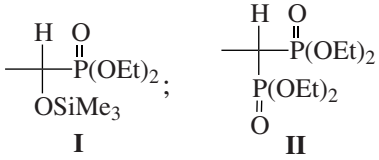
In recent years numerous attempts at structural modification of available antioxidants aimed at increasing their activity have been undertaken. Sterically hindered 2,6-di-*tert*-butylphenols, which possess reducing properties and terminate chain oxidation when they react with peroxyl radicals, are widely used as antioxidants [1, 2]. The combined introduction of these radical inhibitors and hydroperoxide destroying agents (e.g., alkyl or aryl phosphonates) induce effective retardation of oxidative processes in polyolefins, rubbers, lubricating oils, and other materials. Of interest from the practical standpoint is internal synergism, i.e., a situation where the antioxidant molecule contains functional groups of different chemical nature. These polyfunctional antioxidants are exemplified by sterically hindered phosphonates containing groups with different inhibition mechanisms, one fragment terminating chains by accepting $RO_2^{\cdot}$ and the other fragment decreasing the autoinitiation rate by destroying ROOH and complexing metals that destroy hydroperoxides to give free radicals [3].

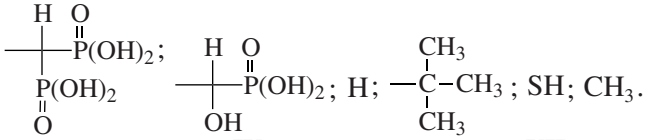
The purpose of this study was to elucidate the effect of phosphorylated phenols on the rate of sturgeon liver lipid peroxidation (LPO) and to compare them with known antioxidants, i.e., sterically hindered phenols under long process conditions.

The antioxidant properties of the following compounds were studied:



where X is 

I **II**



III **IV** **V** **VI** **VII** **VIII**

Determination was carried out by a standard procedure based on accumulation of carbonyl products, determined using thiobarbituric acid, in the female Russian sturgeon liver (*Acipenser guldenstadti* Brandt) in vitro [4]. Organometallic compounds and antioxidants (concentrations 1×10^{-4} mol/L) were introduced into a liver homogenate as chloroform or ethanol solutions; the experiment duration was 3 days.

The efficiency of the antioxidant action (EAA) of the compounds [5] was calculated from the relation

$$\text{EAA} = \frac{C_0 - C_1}{C_0} \times 100\%,$$

where C_0 and C_1 are the malonic dialdehyde (MDA) concentrations in the control and test liver homogenates, respectively.

If the EAA is positive, the test compound shows an antioxidant action; a negative EAA value attests to a prooxidant action.

The EAA of the studied compounds changes considerably during a long-term LPO process in the liver homogenate and depends on the chemical nature of the antioxidant (Table 1).

In the control experiment, the MDA content regularly increased with time. In the initial period of LPO (1–3 h), the most pronounced effect is observed for known antioxidants **V**, **VI**, and **VII**. At far LPO stages, the efficiency of their antioxidant action decreases but no inversion to prooxidant action is observed.

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At medium and far LPO stages, the most pronounced action is exerted by phosphorylated sterically hindered phenols, for which the EAA somewhat increases in the course of the LPO process and decreases at the last stage of investigation. In the series of sterically hindered phosphorylated phenols, compound **III** is most efficient. It is of interest that, at early LPO stages (1 h), these compounds, except compound **II**, exhibit a slight prooxidant action.

To estimate the action of these antioxidants under oxidative stress conditions promoted by mercury and tin organic derivatives, the effect of CH_3HgI, CH_3SnCl_3, $(CH_3)_2SnCl_2$, and $(CH_3)_3SnCl$ additives on the sturgeon liver LPO was considered.

It can be seen in the figure that almost all organomercury and -tin compounds promote LPO processes. The most pronounced promoting action was found for $(CH_3)_2SnCl_2$ and $(CH_3)_3SnCl$ (the MDA concentration increases 1.75- and 1.5-fold, respectively, in the presence of these compounds with respect to the control experiment). Phosphorylated phenols **I–IV** exhibited antioxidant action upon LPO promotion by these toxicants, which is in line with published data indicating a decrease in the promoting effect of organotin compounds on the in vitro oxidation of oleic acid [6]. Note that functional groups in these compounds are able to act as ligands with respect to metals and their compounds. Therefore, a combination of two processes can be expected, namely, inhibition of substrate peroxidation and chelation of metals and metal compounds. From this standpoint, the considered compounds are of interest as potential antioxidant traps with respect to toxic organometallic compounds or products of their decomposition.

The most pronounced inhibition of accumulation of carbonyl products of LPO was found for compound **III**, whose antioxidant action is observed, unlike that in autooxidation, even in the initial LPO stages.

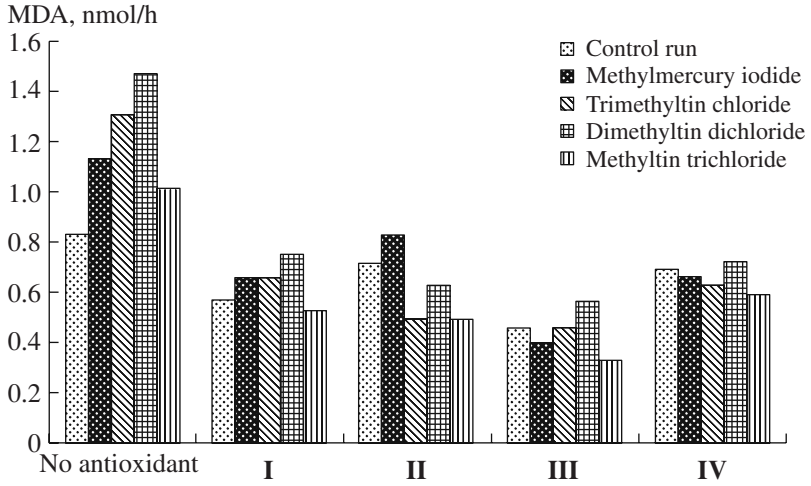
Table 1. EAA of the studied compounds during long-term in vitro oxidation of Russian sturgeon liver lipids

Antioxidant	EAA (%) for long-term oxidation				
	1 h	3 h	24 h	48 h	72 h
I	–1.21	40.6	50	60.9	50.2
II	10.9	35.5	48.1	71.9	68.4
III	–1.22	73.3	75	76.8	61.7
IV	–6.04	48.8	57.6	54.8	54.1
V	48.1	53.8	38.8	26.09	25
VI	56.2	59.9	24.1	22.87	16
VII	48.1	46.1	33.8	21.7	18.7
VIII	35.1	35.4	42.4	38.9	22.9

To simulate the in vitro behavior of compounds **I–IV** during long-term oxidation promoted by $(CH_3)_2SnCl_2$, which is most toxic among the compounds studied here, we studied the dynamics of MDA accumulation during LPO (Table 2).

A noticeable antioxidant action was found for all LPO stages; unlike autooxidation, LPO suppression was observed even in early stages and was somewhat enhanced with an increase in oxidation time. Phosphorylated phenols **I–IV** generally suppressed LPO more efficiently in the case of autooxidation than in the case of toxicant-promoted oxidation.

Thus, we established clear-cut antioxidative activity of phosphorylated phenols, which depends on the chemical structure of the compound and the oxidation duration. A decrease in the promoting action of mercury and tin compounds during long-term LPO in the presence of phosphorylated sterically hindered phenols was demonstrated.



Variation of the accumulation rate of malonic dialdehyde in the Russian sturgeon liver in vitro in the presence of antioxidants and mercury and tin compounds (the average values for a series of experiments are given).

Table 2. EAA of phosphorylated phenols **I–IV** in the presence of $(CH_3)_2SnCl_2$ during long-term in vitro oxidation of Russian sturgeon liver lipids

Compound	EAA (%) for long-term oxidation							
	1 h		3 h		24 h		48 h	
	with a toxicant	autooxidation	with a toxicant	autooxidation	with a toxicant	autooxidation	with a toxicant	autooxidation
$(CH_3)_2SnCl_2$	–46.16		–53.84		–56.66		–62.46	
$(CH_3)_2SnCl_2$ with the addition of								
I	34.24	–1.21	42.49	40.6	48.93	50	49.98	60.9
II	44.73	10.9	52.5	35.5	57.44	48.1	57.68	71.9
III	50	–1.22	55	73.3	63.83	75	67.3	76.8
IV	31.58	–6.04	42.49	48.8	53.18	57.6	51.91	54.8

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