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Synthesis and Investigation of Antioxidant Properties of Alkylated Hydroxybenzyl Dodecyl Sulfides

A. E. Prosenko, O. I. Dyubchenko, E. I. Terakh, A. F. Markov, E. A. Gorokh, and M. A. Boiko

Research Institute of Antioxidant Chemistry, Novosibirsk State Pedagogical Institute, Vilyuiskaya ul. 28, Novosibirsk, 630126 Russia
e-mail: chemistry@ngs.ru

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Abstract—Various alkyl-substituted hydroxybenzyl dodecyl sulfides were synthesized, and a comparative study of their antiradical activity in the model reaction of initiated styrene oxidation and the overall inhibiting activity in the thermal autooxidation of white mineral oil was carried out.

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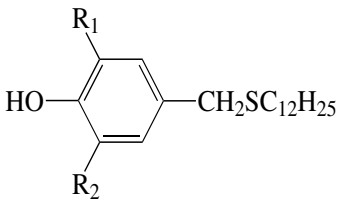
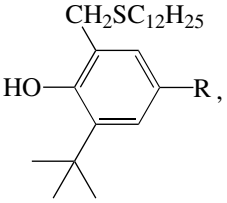
Hydroxybenzyl thio derivatives are high-performance antioxidants capable of preventing the oxidative degradation of different organic materials such as polyolefins, rubbers, lubricating oils, and fuels [1–6] and, thus, improve their performance characteristics and prolong the service life. Of this type of antioxidant, 2,6-di-*tert*-butylphenol derivatives are of the greatest practical importance; this is the reason why most earlier studies have concerned the inhibiting activity and mechanism of antioxidant action of these compounds [7–10]. However, there has been no systematic investigation of the antioxidant activity of 2,6-dialkylsubstituted derivatives that differ in the structure of *ortho*-substituents; neither have the activities of isomeric *ortho*- and *para*-hydroxybenzyl thio derivatives been compared.

In connection with this, we attempted in the present work to synthesize hydroxybenzyl dodecyl sulfides (**I–VII**) of the specified structure by reacting dodecyl mercaptan with corresponding *N,N*-dimethylhydroxybenzylamines obtained earlier [11]. We also investigated their antiradical activity in model reaction of initiated styrene oxidation and the overall inhibiting activity in the thermal autooxidation of white oil.



Structure 1
(**I–V**)



Structure 2
(**VI–VII**)

where 1 $R^1 = R^2 =$ *tert*-Bu (**I**); $R^1 = R^2 =$ Me (**II**); $R^1 = R^2 =$ *cyclo*-C_6H_{11} (**III**); $R^1 =$ Me, $R^2 =$ *tert*-Bu (**IV**); and $R^1 =$ Me, $R^2 =$ *cyclo*-C_6H_{11} (**V**) in structure 1 and R = *tert*-Bu (**VI**) or Me (**VII**) in structure 2.

EXPERIMENTAL

Dodecyl (3,5-di-*tert*-butyl-4-hydroxybenzyl) sulfide (I). A mixture containing 7.0 g (26.60 mmol) of *N,N*-dimethyl-(3,5-di-*tert*-butyl-4-hydroxybenzyl)amine and 5.0 g (24.20 mmol) of dodecyl mercaptan in 30 ml of *o*-xylene was refluxed for 16 h in an argon atmosphere, then cooled and diluted with hydrochloric acid. The organic extract was washed with water and dried over Na_2SO_4. The solvent was evaporated and the residue was distilled in vacuum. The yield of sulfide **I** was 6.5 g (64%), bp 211–214°C (1 mmHg).

Sulfides **II–VII** were obtained in a similar way and were purified by vacuum distillation or chromatographically on silica gel using a 25 : 1 hexane–ether solvent blend.

Proton NMR spectra of the synthesized compounds were recorded on a Bruker DRX500 spectrometer at an operating frequency of 500.13 MHz in

Table 1. Characterization of synthesized compounds

Compound	Bp, °C (1 mmHg)	Mp, °C	Yield, wt %	Elemental analysis data, found/calculated, %			Empirical form	^{1}H NMR, δ ppm
				C	H	S		
I	211–214	tar	64	77.16/77.08	11.61/11.50	7.33/7.62	$C_{27}H_{48}OS$	0.89 t (3H, $S(CH_2)_{11}C\underline{H}_3$), 1.26 s (18H, $(C\underline{H}_2)_9$), 1.43 s (18H, *t*-Bu), 1.56 m (2H, $SCH_2\underline{C}H_2$), 2.42 t (2H, $S\underline{C}H_2$), 3.63 s (2H, $ArCH_2$), 5.09 s (1H, OH), 7.06 s (2H, H_{arom}).
II	197–199	56–57	80	75.03/74.94	10.92/10.78	9.22/9.53	$C_{21}H_{36}OS$	0.86 t (3H, $S(CH_2)_{11}C\underline{H}_3$), 1.24 s (18H, $(C\underline{H}_2)_9$), 1.54 m (2H, $SCH_2\underline{C}H_2$), 2.21 s (6H, Me), 2.40 t (2H, $S\underline{C}H_2$), 3.58 s (2H, $ArCH_2$), 4.54 s (1H, OH), 6.89 s (2H, H_{arom}).
III	–	tar	79	79.05/78.75	11.04/11.09	6.39/6.78	$C_{31}H_{52}OS$	0.89 t (3H, $S(CH_2)_{11}C\underline{H}_3$), 1.25s (18H, $(C\underline{H}_2)_9$), 1.27 m (2H, *cyclo*-$C_6\underline{H}_{11}$), 1.42 m (8H, *cyclo*-$C_6\underline{H}_{11}$), 1.55 m (2H, $SCH_2\underline{C}H_2$), 1.76 m (2H, *cyclo*-$C_6\underline{H}_{11}$), 1.86 m (8H, *cyclo*-$C_6\underline{H}_{11}$), 2.39 t (2H, $S\underline{C}H_2$), 2.70 m (2H, *cyclo*-$C_6\underline{H}_{11}$), 3.63 s (2H, $ArCH_2$), 4.72 s (1H, OH), 6.94 s (2H, H_{arom})
IV	–	tar	76	76.34/76.13	11.31/11.18	8.21/8.47	$C_{24}H_{42}OS$	0.88 t (3t, $S(CH_2)_{11}C\underline{H}_3$), 1.27 s (18H, $(C\underline{H}_2)_9$), 1.39 s (9H, *t*-Bu), 1.54 m (2H, $SCH_2\underline{C}H_2$), 2.22 s (3H, Me), 2.41 t (2H, $S\underline{C}H_2$), 3.60 s (2H, $ArCH_2$), 4.69 s (1H, OH), 6.93 d (1H, H_{arom}, J 2.0 Hz), 7.03 d (1H, H_{arom}, J 2.0 Hz).
V	–	tar	78	77.21/77.17	11.04/10.96	7.69/7.92	$C_{26}H_{44}OS$	0.89 t (3ç, $S(CH_2)_{11}C\underline{H}_3$), 1.25 s (18H, $(C\underline{H}_2)_9$), 1.29 m (1H, *cyclo*-$C_6\underline{H}_{11}$), 1.41 m (4H, *cyclo*-$C_6\underline{H}_{11}$), 1.54 m (2H, $SCH_2\underline{C}H_2$), 1.75 m (1H, *cyclo*-$C_6\underline{H}_{11}$), 1.84 m (4H, *cyclo*-$C_6\underline{H}_{11}$), 2.22 s (3H, Me), 2.39 t (2H, $S\underline{C}H_2$), 2.74 m (1H, *cyclo*-$C_6\underline{H}_{11}$), 3.60 s (2H, $ArCH_2$), 4.58 s (1H, OH), 6.90 d (1H, H_{arom}, J 1.5 Hz), 6.93 d (1H, H_{arom}, J 1.5 Hz).
VI	200–202	tar	71	77.19/77.08	11.65/11.50	7.29/7.62	$C_{27}H_{48}OS$	0.92 t (3H, $S(CH_2)_{11}C\underline{H}_3$), 1.30 s (27H, $(C\underline{H}_2)_9$, *t*-Bu), 1.45 s (9H, *t*-Bu), 1.55 m (2H, $SCH_2\underline{C}H_2$), 2.39 t (2H, $S\underline{C}H_2$), 3.82 s (2H, $ArCH_2$), 6.85 s (1H, OH), 6.92 d (1H, H_{arom}, J 2.5 Hz), 7.26 d (1H, H_{arom}, J 2.5 Hz).
VII	195–198	tar	76	76.22/76.13	11.31/11.18	8.12/8.47	$C_{24}H_{42}OS$	0.89 t (3H, $S(CH_2)_{11}C\underline{H}_3$), 1.29 s (18H, $(C\underline{H}_2)_9$), 1.40 s (9H, *t*-Bu), 1.53 m (2H, $SCH_2\underline{C}H_2$), 2.25 s (3H, Me), 2.39 t (2H, $S\underline{C}H_2$), 3.76 s (2H, $ArCH_2$), 6.73 d (1H, H_{arom}, J 2.0 Hz), 6.86 s (1H, OH), 7.03 d (1H, H_{arom}, J 2.0 Hz).

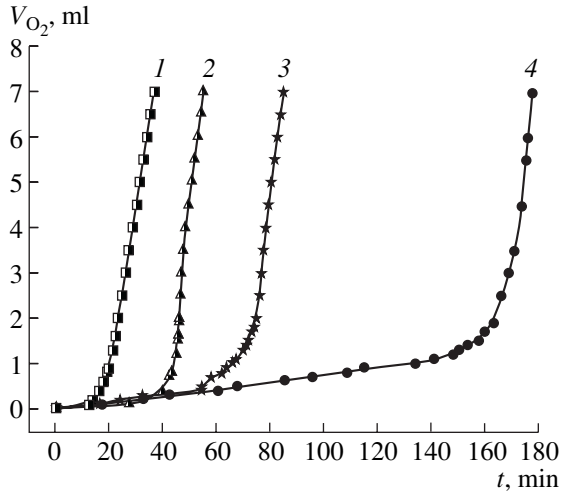


Fig. 1. Rate curves for oxidation of white oil in the presence of (*1*) sulfide **I**, (*2*) ionol, (*3*) SO-3, and (*4*) sulfide **IV**.

$CDCl_3$ with TMS as an internal standard. Melting points were determined with a PTP device.

The physicochemical properties of synthesized compounds are listed in Table 1. Searching in the STN International net showed that compounds **II**, **III**, **V**, and **VII** are new, as they have not been described previously.

The inhibiting activity of sulfides **II**–**VII** was studied in the model reactions of azobisisobutyronitrile (AIBN, Acros Organics, 98%)-initiated oxidation of styrene (chemically pure grade) in chlorobenzene (chemically pure, 99%) at 50°C and thermal autooxidation of white mineral oil (KPKhFO "Takhimfarmpreparaty", Kazan; a density of 0.86, a pour point of at most –5°C) at 180°C; the results were compared with the action of 2,6-di-*tert*-butyl-4-methylphenol (ionol) (Acros Organics), 2,4,6-trimethylphenol (TMP) (Lancaster), as well as bis(3,5-di-*tert*-butyl-4-hydroxybenzyl) sulfide (TB-3) and bis[3-(3,5-di-*tert*-butyl-hydroxyphenyl)propyl] sulfide (SO-3) prepared as described in [12, 13]. Styrene and chlorobenzene were distilled prior to use.

The rate of styrene oxidation was determined by measuring oxygen uptake with a highly sensitive capillary volumeter. The induction period was determined as a crossing point of two tangents to a kinetic curve, whose slopes are 0.5 and 0.75 of the slope of the straight line for the uninhibited reaction [14].

The initiation rate w_i was determined by the method of inhibitors in terms of the length of the induction period of styrene oxidation in the presence of ionol and TMP for which stoichiometric inhibition factor f defined as the average number of oxidation

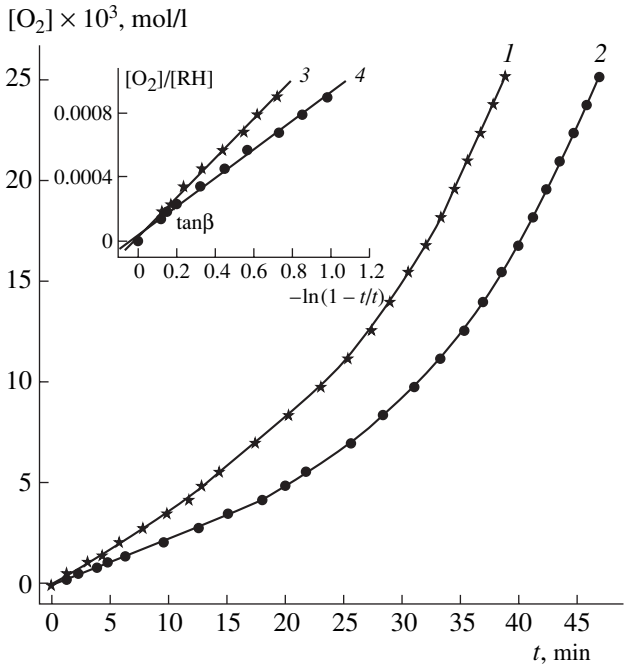


Fig. 2. Oxygen uptake rate curves in the initiated oxidation of styrene at 50°C in the presence of 0.3 mmol/l of sulfides (*1*) **I** and (*2*) **II** and their linear transforms *3* and *4*, respectively.

chains terminated by one phenoxy group of the inhibitor molecule is 2 [11]:

$$w_i = \frac{2[\mathrm{PhOH}]_0}{\tau},$$

where $[\mathrm{PhOH}]_0$ is the initial ionol concentration and τ is the induction period. The determined value of w_i was $(2.7–4.0) \times 10^{-7}$ l mol^{-1} s^{-1}.

The oxidation of white oil was carried out in a gasometric unit similar to the one described in [14], at an oxygen pressure of 1 atm. The total sample volume was 5 ml, and the antioxidant concentration was 1.75 μmol per 1 g of oil. On the basis of the obtained data, kinetic curves were further constructed (Fig. 1), which were used to determine the induction period as the intersection point of two tangents to a kinetic curve corresponding to the initial and final rates of oxidation of the oil.

RESULTS AND DISCUSSION

It was found that the initial portions of kinetic curves for oxygen uptake in styrene oxidation are linearized well in the coordinates of the following equation (1) for all of the test compounds:

$$\frac{\Delta[O_2]}{[RH]} = -\frac{k_2}{k_7}\ln\left(1 - \frac{t}{\tau}\right), \quad (1)$$

where $\Delta[O_2]$ is the amount of absorbed oxygen divided by the sample volume, k_7 and k_2 are the rate constants

Table 2. Antioxidant properties of hydroxybenzyl dodecyl sulfides

Compound	$k_7 \times 10^4$, $mol^{-1}s^{-1}$	τ, min
I	3.0 ± 0.4	17 ± 2
II	11.2 ± 1.3	305 ± 5
III	14.5 ± 3.5	257 ± 8
IV	13.5 ± 2.5	172 ± 7
V	10.0 ± 1.0	284 ± 8
VI	10.0 ± 1.0	80 ± 7
VII	11.0 ± 1.0	48 ± 5
TB-3	2.6 ± 0.4	16 ± 2
SO-3	2.4 ± 0.4	72 ± 5
Ionol	2.6 ± 0.6	43 ± 3
TMP	17.4 ± 2.3	43 ± 5
BDS	–	7 ± 2
Control	–	7 ± 2

Table 3. Synergistic effect of mixed compositions of alkylphenols and benzyl dodecyl sulfides in oxidation of white oil

Phenol*	[BDS], μmol/g	[PhOH] : [BDS] mole ratio	τ, min	$\Delta\tau_{syn}$, min
Ionol	0.00	1 : 0	43	–
	0.88	1 : 0.5	50	0
	1.75	1 : 1	50	0
	3.50	1 : 2	61	11
	4.38	1 : 2.5	74	24
	5.25	1 : 3	199	149
TMP	0.00	1 : 0	43	–
	0.88	1 : 0.5	50	0
	1.75	1 : 1	50	0
	2.63	1 : 1.5	209	159
	3.50	1 : 2	308	258

* [PhOH] = 1.75 μmol/g.

of the reaction of peroxide radicals with antioxidant molecules and the oxidation substrate, respectively; τ is the induction period; *t* is the time; and [RH] is the substrate concentration in the sample.

The obedience to Eq. (1) suggests that the inhibition of styrene oxidation follows the conventional scheme [14] and the rate constant k_7 for the reaction of inhibitors with styrene peroxide radicals can be determined by means of this equation.

Figure 2 depicts oxygen consumption rate curves for compounds **II** and **III** and their transformations in the variables of Eq. (1). The k_2/k_7 ratio was determined from the slope of the transforms (tan β). According to published data [15], the rate constant k_2 in the given model system is 107.7 l mol^{-1} s^{-1}; hence, k_7 = 107.7/tan β. Table 2 presents the values of k_7 for the test antioxidants; the values are given with the mean-square deviation.

From the data presented in Table 2, it follows that all test compounds exhibit a marked reactivity towards styrene peroxide radicals; their mean values of the rate constant k_7 vary in the range $(2.4–17.4) \times 10^4$ l mol^{-1} s^{-1}. The rate constants k_7 for sulfur-containing alkylphenols–sulfides **I** and **II**, TB-3, and SO-3—are practically the same as those for the corresponding monofunctional antioxidants ionol and TMP. Of the test *para*-substituted derivatives, compounds with di-*tert*-butyl *ortho*-substituents have values of the rate constant k_7 3.3–7.3 times lower than their less hindered analogues, phenols with dimethyl, dicyclohexyl, methyl-*tert*-butyl, and methylcyclohexyl *ortho*-substitution, in agreement with the known literature data [10]. In addition, these di-*tert*-butylphenols display a lower antiradical activity in comparison with *ortho*-benzyl substituted sulfides **VI** and **VII**.

The overall inhibiting activity of sulfides **I–VII** in comparison with reference antioxidants was evaluated as their ability to retard the oxidation of white oil. The results of the investigation show that all synthesized sulfides increase the stability of white oil against oxidation (Table 2); however, different compounds demonstrate different inhibiting effects.

Among the synthesized compounds, sulfides **II–V** display the highest antioxidant activity and are superior to ionol and TMP, as well as to sulfur-containing alkylphenols SO-3 and TB-3, in their inhibiting effect. The lowest inhibiting activity was demonstrated by sulfide **I**, which significantly weaker retards the oxidation of white oil in comparison with other synthesized compounds. Note that TB-3, the symmetric analogue of sulfide **I**, also exhibits a low antioxidant activity comparable with that of this sulfide.

We associate the high antioxidant activity of sulfides **II–VI** first with the bifunctional mechanism of their antioxidant action and, second, with an intramolecular synergistic effect. These compounds can exhibit a bifunctional activity due to combination of the antirad-

ical activity of the phenolic OH group, which inactivates peroxide radicals (Table 2), with the antiperoxide activity of the sulfur-containing moiety capable of acting as a destroyer of peroxide compounds. The existence of the intramolecular synergistic effect is due to the specific features of the molecular structure of the inhibitors, which enhance their antioxidant activity.

The evidence that sulfides **II–VI** are bifunctional inhibitors stems from the fact that they are superior to monofunctional antioxidants in their total inhibiting activity. Since monofunctional antioxidants can retard the oxidation process only as a result of interaction with peroxide radicals, the higher antioxidant activity of sulfides **II–VI** may be attributed only to the additional antioxidant activity of the sulfide moiety.

To reveal the existence of the intramolecular synergistic effect, as well as to explain the considerable difference in the activity between the most effective inhibitor dimethyl substituted sulfide **II** and di-*tert*-butyl substituted sulfide **I** having an extremely low antioxidant activity, we studied the inhibiting activity of the compositions of alkylphenols (using ionol and TMP as an example) with admixed benzyl dodecyl sulfide (BDS).

The obtained data showed the absence of synergy for the compositions with phenol to sulfide molar ratios of 1 : 0.5 and 1 : 1 (Table 3). The intermolecular synergistic effect in the case of joint use of alkylphenols and BDS has been revealed at a higher amount of the sulfide component in the mixture and is evaluated by the quantity $\Delta\tau_{syn}$:

$$\Delta\tau_{syn} = \tau_{PhOH + BDS} - (\tau_{BDS} + \tau_{PhOH})$$

where τ_{BDS} and τ_{PhOH} are the induction periods in the oxidation of white oil in the presence of BDS and alkylphenols as individual compounds, respectively, and $\tau_{PhOH + BDS}$ is the induction period of white oil oxidation in the presence of mixed alkylphenol–BDS compositions.

The lack of synergistic effect for alkylphenol compositions with BDS at component molar ratios of 1 : 0.5 and 1 : 1 is obviously due to the fact that the added amount of BDS is insufficient to inactivate the peroxide compounds formed during the oxidation of oil. An increase in the BDS concentration results in a more complete inactivation of the peroxides, thus creating conditions for the appearance of the synergistic effect.

In contrast to the mix composition TMP and BDS (1 : 1 by mole), the value of the induction period is 6.0 times the sum of induction periods of the individual antioxidants TMP and BDS in the presence of dimethyl substituted sulfide **II**. Such a high value is indicative of a strong synergistic effect of sulfide **II**, which is intramolecular in nature.

In the case of sulfide **I** and its symmetric analogue TB-3, the synergistic effect was undetectable. On the contrary, the total inhibiting effect in the presence of ionol and BDS was 3.0 times that exhibited by sulfide **I** and TB-3. It is known [17] that antioxidant mixtures can exhibit not only synergism but also antagonism; thus, sulfide **I** and TB-3 seem to display intramolecular antagonism under the given conditions. The reasons behind this phenomenon are unclear; however, the appearance of intramolecular antagonism may be associated, e.g., with the formation during oxidation of thermally unstable products that act as a source of free radicals taking part in the propagation of oxidation chains.

From the data obtained by studying the antioxidant activity of mixed compositions of alkylphenols with BDS, it follows that the extent of intermolecular synergistic effect depends not only on the BDS concentration but also on the structure of the phenolic component. For example, the compositions containing TMP as a phenolic component exhibit a higher inhibiting activity than compositions on the basis of ionol. This finding suggests that the degree of intramolecular synergism may differ for compounds with different structures of the phenol moiety. It is obviously for this reason that sulfides **II–VII** display different inhibiting activities.

In general, the results of the investigation show that hydroxybenzyl dodecyl sulfides synthesized in this work exhibit a distinct antiradical activity toward styrene peroxide radicals, as well as a high inhibiting effect in the thermal autooxidation of white mineral oil. Owing to the bifunctional mechanism of antioxidant action and the presence of the intramolecular synergistic effect, some sulfides are superior in their inhibiting activity to the well-known antioxidants ionol and TMP, as well as to sulfur-containing alkylphenols SO-3 and TB-3. Among these compounds, dimethyl and methyl cyclohexyl substituted sulfides display the highest antioxidant activity, inhibiting the oxidation processes 4.0–19.0 times more effectively than the reference antioxidants.

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