UDC 547+544

Synthesis and Antioxidant Properties of ω-[3-(4-Hydroxyaryl)propylthio]alkanic Acids

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Abstract

On the basis of bromopropyl-, mercaptopropyl- and allyl-substituted phenols, the synthesis of ω-[3-(4-hydroxyaryl)propylthio]alkanoic acids was carried out. It was shown in the model reaction of methyl oleate autooxidation that the synthesized ω-[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylthio]alkanoic acids exceed phenosan antioxidant in the antioxidant activity due to the presence of sulphide groups in their structure.

Key words: phenols, polyfunctional antioxidants, thioalkanoic acids, phenosan, antioxidant activity

INTRODUCTION

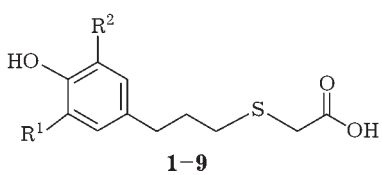
It has been reliably established by present that an increase in the intensity of free radial oxidation in living organisms (oxidative stress) causes the formation and development of a wide range of diseases and pathologies [1]. This defines the urgency of search for antioxidants for efficient prophylactics and correction of pathophysiological effects of the oxidative stress.

Phenosan is antioxidant preparation promising for use in biology and medicine. Within a broad concentration range, this compound exhibits clearly pronounced biological activity, in particular antitumour [2] and radioprotective [3, 4] properties, anticonvulsant and nootropic action [5]. On the other hand, phenol compounds having a bivalent sulphur atom in their structure are considered as efficient bioantioxidants. For instance, as a rule, these compounds exceed analogues containing no sulphur in the ability to inhibit oxidation in biological systems [6–8].

In this connection, in the present work we carried out the synthesis and comparative studies of the antioxidant properties of sulphur-containing analogues of phenosan – ω-[3-(4-hydroxyaryl)propylthio]alkanoic acids **1–10** (Scheme 1).

EXPERIMENTAL

Compounds **1–10** were synthesized from 3-(4-hydroxyaryl)-1-bromopropanes [9], 4-allyl-



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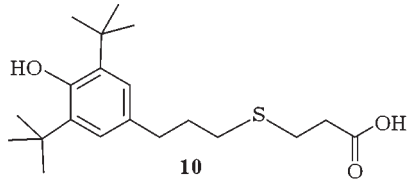

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$R^1 = R^2 = t$-Bu (**1**), H (**2**), Me (**3**), *cyclo*-C_6H_{11} (**4**); R^1 = Me, $R^2 = t$-Bu (**5**), *cyclo*-C_6H_1 (**6**); R^1 = H, R^2 = OMe (**7**), t-Bu (**8**), *cyclo*-C_6H_{11} (**9**).

Scheme 1.

2,6-dialkylphenols [9, 10], 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propanethiol-1 [11, 12] and 4-allyl-2-methoxyphenol (Aldrich) in reactions with commercial acids: 2-mercaptoethanoic (Russia), 2-chloroethanoic (Russia) and 3-bromopropanoic (Merck).

2-[3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propylthio]ethanoic acid (1). To the solution of 5 g (15.3 mmol) of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1-bromopropane in 25 mL of ethanol, in the atmosphere of argon, we added 2 g (50 mmol) NaOH and 2.1 g (22.8 mmol) of 2-mercaptoethanoic acid in 15 mL of water, then heated the reaction mixture under mixing for 4 h at 40 °C. Then the reaction mixture was cooled, neutralized with HCl, treated with toluene, the extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was washed with warm hexane and dried. The target acid **1** was obtained in the amount of 4.51 g (87 %) (Table 1).

A similar procedure was used to synthesize 2-[3-(4-hydroxyphenyl)propylthio]ethanoic acid **2**, 2-[3-(4,5-dimethyl-4-hydroxyphenyl)-propylthio]ethanoic acid **3**, 2-(3-(3-*tert*-butyl-4-hydroxyphenyl)propylthio]ethanoic acid **8**, 2-[3-(3-cyclohexyl-4-hydroxyphenyl)propylthio]ethanoic acid **9**.

2-[3-(3,5-Dimethyl-4-hydroxyphenyl)-propylthio]ethanoic acid (3). A mixture of 5 g (30.8 mmol) of 2,6-dimethyl-4-allylphenols, 4.25 g (46.2 mmol) of 2-mercaptoethanoic acid and 0.52 g (1.85 mmol) of 4,4′-azo-*bis*(4-cyanovaleric acid) (ACVA, Aldrich) was heated and stirred for 4 h at 120 °C under argon. The reaction mass was cooled and treated with toluene. The extract was washed with aqueous NaCl, and then treated with aqueous KOH solution (1.7 g (30 mmol) of KOH in 40 mL of water). The alkaline extract was separated, acidified and then treated with toluene. The extract was washed with water until neutral reaction of water, dried with Na_2SO_4, the solvent was distilled off. The target acid **3** was obtained in the amount of 5.67 g (82 %).

The same procedure was used to synthesize 2-[3-(3,5-dicyclohexyl-4-hydroxyphenyl)-propylthio]-ethanoic acid **4**, 2-[3-(3-methyl-5-*tert*-butyl-4-hydroxyphenyl)propylthio]ethanoic acid **5**, 2-[3-(3-methyl-5-cyclohexyl-4-hydroxyphenyl)-propylthio]ethanoic acid **6**, 2-[3-(3-methoxy-4-hydroxyphenyl)propylthio]ethanoic acid **7**.

3-[3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propylthio]propanoic acid (10). To the solution of 5 g (17.8 mmol) of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1-propanethiol-1 in 20 mL of ethanol, we added 1.93 g (48.2 mmol) NaOH in 15 mL of water, then 4.1 g (25.5 mmol) of 3-promopropanoic acid. The mixture was heated and mixed for 4 h at 40 °C. Then the reaction mixture was cooled, neutralized with HCl, treated with toluene, the extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The target acid **10** was obtained in the amount of 5.76 g (92 %).

The ^{1}H NMR spectra were recorded with a Bruker DRX500 spectrometer with the working frequency of 500.13 MHz: for compounds **1**, **3**–**10** in $CDCl_3$ with respect to $CHCl_3$, for compound **2** in D_2O with respect to $Si(CH_3)_4$. Melting points were measured using the PTP instrument (Russia).

Oxidation of methyl oleate (Acros Organics) was carried out in the air at 60 °C. The mass of the sample under oxidation was 5 g, the concentration of the compounds under investigation was 1 mmol/g. During the experiment, samples of 0.1 g were taken, and the concentrations of peroxide compounds were measured using the ferric thiocyanate method according to the procedure described in [13], with the help of a Specord UV Vis spectrophotometer. The time within which the peroxide number equal to 0.05 % I_2 was achieved was taken as the induction period. The initial peroxide number (PN) of methyl oleate was 0.002 %. The reference antioxidant was 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propanoic acid (phenosan, NII Khimpolimer, Russia).

Plotting and mathematical processing of kinetics curves were carried out using the Origin 6.0 software.

The antiperoxide activity of the synthesized compounds was assessed as their effect on the kinetics of cumene hydroperoxide decomposition (CHP, Aldrich) at 60 °C. Experiments were carried out in glacial acetic acid (Russia) with the initial concentration of CHP equal to 0.01 mol/L. The degree of CHP decomposition was controlled using the ferric thiocyanate method according to the procedure described in [13].

TABLE 1

Yields, melting points, the data of elemental analysis and ^{1}H NMR spectra for synthesized compounds

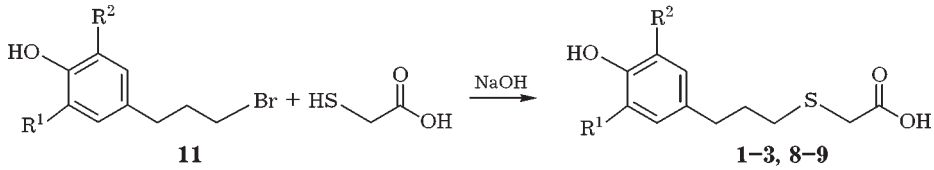
Compounds	Yield, %	T_m, °C	Elemental analysis[a], %			Gross formula	^{1}H NMR spectra, δ, ppm
			C	H	S		
1	87[b]	Tar	67.62/67.42	9.00/8.93	9.74/9.47	$C_{19}H_{30}O_3S$	1.46 s (18H, *t*-Bu), 1.92 m (2H, $ArCH_2C\underline{H}_2$), 2.64 t (2H, $ArC\underline{H}_2$, *J* 7 Hz), 2.71 t (2H, $Ar(CH_2)_2C\underline{H}_2$, *J* 7 Hz), 3.21 s (2H, $C\underline{H}_2COOH$), 4.95 br. s (1H, $ArO\underline{H}$), 6.92 c (2H, H_{arom}), 11.86 br. s (1H, COOH)
2	77[b]	93–95	58.15/58.38	6.07/6.24	14.36/14.17	$C_{11}H_{14}O_3S$	2.16 m (2H, $ArCH_2C\underline{H}_2$), 2.93 m (4H, $ArC\underline{H}_2CH_2C\underline{H}_2$), 3.65 s (2H, $C\underline{H}_2COOH$), 7.15 d (2H, H_{arom}, *J* 8.5 Hz), 7.44 d (2H, H_{arom}, *J* 8.5 Hz)
3	89[b] 82[c]	67–69	61.19/61.39	7.07/7.13	12.90/12.60	$C_{13}H_{18}O_3S$	1.85 m (2H, $ArCH_2C\underline{H}_2$), 2.20 s (6H, Me), 2.57 m (4H, $C\underline{H}_2CH_2C\underline{H}_2$), 3.19 s (2H, $C\underline{H}_2COOH$), 4.95 s (1H, $ArO\underline{H}$), 6.74 s (2H, H_{arom})
4	94[c]	Tar	70.84/70.73	8.73/8.77	8.29/8.21	$C_{23}H_{34}O_3S$	1.29 m (2H, *cyclo*-C_6H_{11}), 1.41 m (8H, *cyclo*-C_6H_{11}), 1.85 m (10H, *cyclo*-C_6H_{11}, 2H, $ArCH_2C\underline{H}_2$), 2.62 m (4H, $ArC\underline{H}_2CH_2C\underline{H}_2$, 2H, *cyclo*-$C_6H_{11}$), 3.23 s (2H, $C\underline{H}_2COOH$), 6.71 s (2H, H_{arom})
5	88[c]	Tar	64.81/64.83	8.24/8.16	10.89/10.82	$C_{16}H_{24}O_3S$	1.41 s (9H, *t*-Bu), 1.89 m (2H, $ArCH_2C\underline{H}_2$), 2.21 s (3H, Me), 2.60 t (2H, $ArC\underline{H}_2$, *J* 7 Hz), 2.67 t (2H, $Ar(CH_2)_2C\underline{H}_2$, *J* 7 Hz), 3.19 s (2H, $C\underline{H}_2COOH$), 4.00-6.00 br. s (1H, $ArO\underline{H}$), 6.75 d (2H, H_{arom}, *J* 2 Hz), 6.87 d (2H, H_{arom}, *J* 2 Hz), 8.00–13.00 br. s (1H, COOH)
6	92[c]	Tar	67.11/67.05	8.23/8.13	9.89/9.94	$C_{18}H_{26}O_3S$	1.23 m (1H, *cyclo*-C_6H_{11}), 1.42 m (4H, *cyclo*-C_6H_{11}), 1.83 m (5H, *cyclo*-C_6H_{11}, 2H, $ArCH_2C\underline{H}_2$), 2.18 s (3H, Me), 2.57 t (2H, $ArC\underline{H}_2$, *J* 7 Hz), 2.63 t (2H, $Ar(CH_2)_2C\underline{H}_2$, *J* 7 Hz), 2.71 m (1H, *cyclo*-C_6H_{11}), 3.15 s (2H, $C\underline{H}_2COOH$), 6.68 d (1H, H_{arom}, *J* 2 Hz), 6.73 d (1H, H_{arom}, J 2 Hz
7	85[c]	Tar	56.19/56.23	6.33 6.29	12.48/12.51	$C_{12}H_{16}O_4S$	1.88 m (2H, $ArCH_2C\underline{H}_2$), 2.62 m (4H, $ArC\underline{H}_2CH_2C\underline{H}_2$), 3.18 s (2H, $C\underline{H}_2COOH$), 3.84 s (3H, OMe), 6.60 m (2H, H_{arom}), 6.75 d (1H, H_{arom}, *J* 8.5 Hz), 8.00–13.00 br. (2H, OH, COOH)
8	75[b]	Tar	63.56/63.80	7.76/7.85	11.71/11.35	$C_{15}H_{22}O_3S$	1.38 s (9H, *t*-Bu), 1.88 m (2H, $ArCH_2C\underline{H}_2$), 2.62 t (2H, $ArC\underline{H}_2$, *J* 7 Hz), 2.61 t (4H, $Ar(CH_2)_2C\underline{H}_2$, *J* 7 Hz), 3.23 s (2H, $C\underline{H}_2COOH$), 6.55 d (1H, H_{arom}, *J* 8 Hz), 6.85 dd (1H, H_{arom}, *J* 8 Hz, *J* 2 Hz), 7.03 d (1H, H_{arom}, *J* 2 Hz)
9	85[b]	96–98	66.33/66.20	7.68/7.84	10.25/10.39	$C_{17}H_{24}O_3S$	1.27 m (1H, *cyclo*-C_6H_{11}), 1.41 m (4H, *cyclo*-C_6H_{11}), 1.75 m (1H, *cyclo*-C_6H_{11}), 1.84 m (4H, *cyclo*-C_6H_{11}), 1.89 m (2H, $ArCH_2C\underline{H}_2$), 2.63 t (2H, $ArC\underline{H}_2$, *J* 7 Hz), 2.66 t (2H, $Ar(CH_2)_2C\underline{H}_2$, *J* 7 Hz), 2.79 m (1H, *cyclo*-C_6H_{11}), 3.25 s (2H, $C\underline{H}_2COOH$), 6.66 d (1H, H_{arom}, *J* 8 Hz), 6.85 dd (1H, H_{arom}, *J* 8 Hz, *J* 2 Hz), 6.97 d (1H, H_{arom}, *J* 2 Hz)
10	92[d]	95–97 (94–95 [14])	68.01/68.14	9.27/9.15	9.39/9.09	$C_{20}H_{32}O_3S$.	1.42 s (18H, *t*-Bu), 1.87 m (2H, $CH_2C\underline{H}_2CH_2$), 2.56 t (2H, $Ar(CH_2)_2C\underline{H}_2$, *J* 7 Hz), 2.60 t (2H, $ArC\underline{H}_2$, *J* 7 Hz), 2.64 t (2H, $C\underline{H}_2CH_2COOH$, *J* 7 Hz),2.77 t (2H, $C\underline{H}_2COOH$, *J* 7 Hz), 5.04 s (1H, $ArO\underline{H}$), 6.96 s (2H, H_{arom})

[a] The first value: found, the second: calculated.

[b] Target acids **1**–**10** were obtained from 3-(4-hydroxyaryl)-1-bromopropanes.

[c] Target acids **1**–**10** were obtained from 4-allyl-2,6-dialkylphenols.

[d] Target acids **1**–**10** were obtained from 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propanethiol-1.



$R^1 = R^2 = t$-Bu (**1**), H (**2**), Me (**3**), R^1 = H, $R^2 = t$-Bu (**8**), *cyclo*-C_6H_{11} (**9**)

Scheme 2.

RESULTS AND DISCUSSION

Compounds **1**–**10** were synthesized using different approaches; their choice was made taking into account the availability of initial compounds.

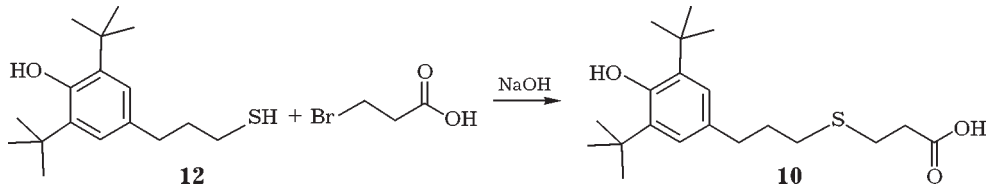
Acids **1**–**3** and **8**, **9** were synthesized in the reactions of the corresponding bromopropylphenols **11** with 2-mercaptoethanoic acid (Scheme 2).

Syntheses were carried out in the presence of NaOH because thiolate ions RS^- that are formed in the alkaline medium exceed in the nucleophilic strength the corresponding RSH thiols. In addition, a 1.5-fold excess of mercaptoethanoic acid was introduced into the reaction in order to prevent the side reaction which was the condensation of bromopropylphenols as a consequence of the attack of phenolate ions at the C–Br bond. Under these conditions, independently of the number and structure of *ortho*-substituents in the molecules of brominated derivatives **11**, their interaction with 2-mercaptoethanoic acid proceeded smoothly and resulted in the formation of target products with high yields (75–89 %).

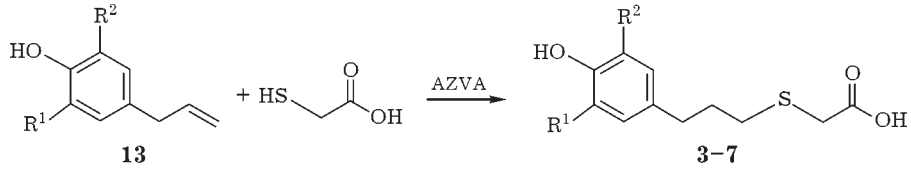
Under similar conditions, thiopropanoic acid **10** was synthesized from thiol **12** and 3-bromopropanoic acid with the yield of 92 % (Scheme 3).

It should be noted that our attempts to synthesize acid **1** according to the reaction of thiol **12** with 2-chloroethanoic acid turned out to be less successful. We failed to achieve complete conversion of thiol **12** either by increasing the molar excess of chloroethanoic acid to 4-fold or by an increase in the time of mixture heating to 6–7 h: the yield of acid 1 was 68 % at the best. This result is likely due to the fact that the negatively charged group in the $ClCH_2COO^-$ anion is directly connected with the carbon atom at which the nucleophilic attack of thiolate is directed.

The synthesis of some ω-[3-(3,5-dialkyl-4-hydroxyaryl)propylthio]alkanoic acid was described previously in [14]. Unlike the authors of that work, we carried out the interaction of allyl phenols **13** with 2-mercaptoethanoic acid using another azo initiator, and the yield of target thioethanoic acids **3**–**7** was 82–94 % (Scheme 4).



Scheme 3.



$R^1 = R^2$ = Me (**3**), *cyclo*-C_6H_{11} (**4**); R^1 = Me, $R^2 = t$-Bu (**5**), *cyclo*-C_6H_{11} (**6**); R^1 = H, R^2 = OMe (**7**)

Scheme 4.

The ability of synthesized compounds **1**–**10** to inhibit the oxidation of lipid substrates was studied in the model reaction of methyl oleate autooxidation at 60 °C. Phenosan was used as the reference compound.

According to the data obtained (Fig. 1, *a*), in the model system under consideration, the synthesized thioethanoic acids **1**–**9** possess substantially differing antioxidative activity: in the concentration of 1 mmol/g they caused an increase in the induction period of methyl oleate autooxidation by a factor of 2–93, the least efficient inhibitor being *ortho*-unsubstituted acid **2**, while the most efficient inhibitor was *ortho*-di-*tert*-butyl-substituted acid **1**. Sequential removal of *tert*-butyl *ortho*-substituents in the row of compounds **1**–**8**–**2**, replacement of *tert*-butyl substituents by methyl ones in the row **1**–**5**–**3**, and by cyclohexyl when passing from **1** to **4**, from **5** to **6** and from **8** to **9** caused a decrease in the efficiency of antioxidant action.

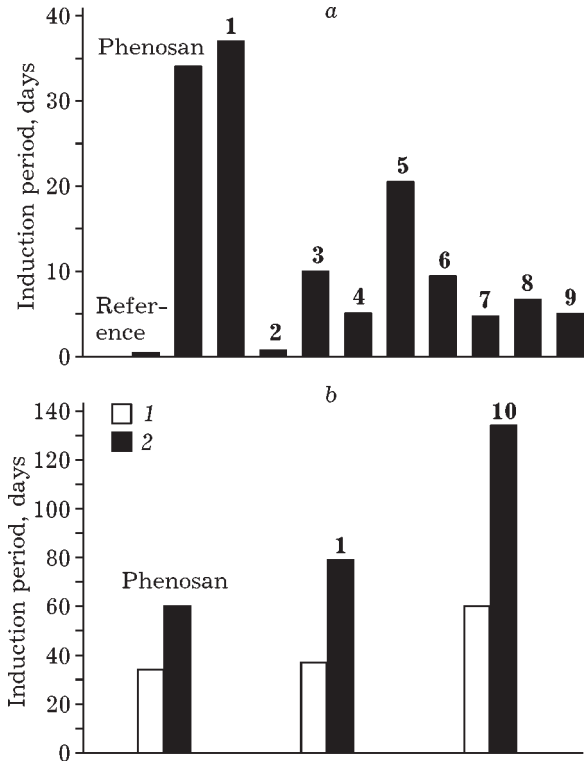


Fig. 1. Diagram of induction periods of methyl oleate oxidation (60 °C) inhibited with phenosan and various acids: *a* – 2-[3-(4-hydroxyaryl)propylthio]ethanoic **1**–**9** (1 mmol/g), *b* – ω-[3-(di-*tert*-butyl-4-hydroxyphenyl)propylthio]-alkanoic **1**, **10**; concentration, mmol/L: 1 (*1*), 2 (*2*).

It is known that the antioxidant activity of phenol compounds (ArOH) is based on their ability to interact with active radicals including lipoperoxide ones ($LOO^{\bullet}$), with the formation of stable phenoxyl radicals ($ArO^{\bullet}$):

$$ArOH + LOO^{\bullet} \rightarrow ArO^{\bullet} + LOOH \quad (1)$$

Changes in the number and structure of *ortho*-substituents cause, on the one hand, changes in the reactivity of phenols in reaction (1); on the other hand, changes in the stability of phenoxyl radicals and the probability of their participation in the stages of propagation of oxidation chains:

$$ArO^{\bullet} + LH \rightarrow ArOH + L^{\bullet} \quad (2)$$

In this situation, the reactivity of phenoxyls in reaction (2) increases substantially with a decrease in the screening effect of *ortho*-substituents [15].

It was demonstrated previously [10] that 4-(3-alkylthiopropyl)phenols containing *tert*-butyl, methyl and cyclohexyl groups in *ortho*-positions are characterized by the close rate constants of their interaction with lipoperoxide radicals of methyl oleate. Thus, a decrease in the efficiency of the inhibiting action with respect to methyl oleate autooxidation in the series of thioethanoic acids **1**–**9** with a decrease in the degree of spatial screening of the phenol OH group is due mainly to a decrease in the stability of the corresponding phenoxyl radicals.

The compounds with the same type of *ortho*-substitution – thioalkanoic acids **1**, **10** and phenosan – in the model system under consideration also differed from each other in the antioxidant activity (see Fig. 1, *b*).

Unlike phenosan, acids **1**, **10** in their molecular design are antioxidants with the bifunctional principle of action: along with the phenol fragment possessing antiradical activity, they also contain sulphhydryl group able to reduce the precursors of active radicals – lipoperoxides. This implies higher antioxidant activity of these compounds. At the same time, in the concentration of 1 mmol/g phenosan and thioethanoic acid 1 inhibited methyl oleate autooxidation with similar efficiency, while in the concentration of 2 mmol/g thioethanoic acid **1** exceeded phenosan in efficiency only by a factor of 1.3. In the same concentrations, the duration of inhibition of methyl oleate oxidation by thiopropanoic acid **10** exceeded that for phe-

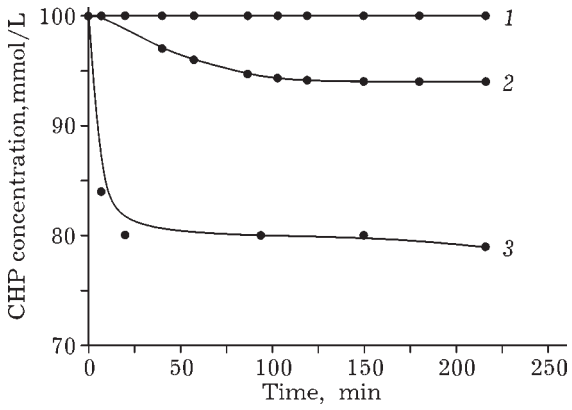


Fig. 2. Kinetic curves of cumene hydroperoxide (CHP) decomposition in the presence of 0.01 M phenosan (*1*) and ω-[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylthio]alkanoic acids **1**, **10** (*2*, *3*) at 60 °C.

nosan by a factor of 1.8–2.2 and that for thioethanoic acid 1 by a factor of 1.6–1.7.

In order to reveal possible reasons of the differences in the efficiency of the antioxidant action of acids **1**, **10**, we carried out comparative evaluation of their antiperoxide activity in the model reaction of cumene hydroperoxide (CHP) decomposition [16].

According to the data obtained (Fig. 2), exposure if the 0.1 M solution of CHP in acetic acid at 60 °C for 4 h did not cause any change in the concentration of hydroperoxide, and the addition of phenosan into the system did not affect the stability of CHP. Under the same conditions in the presence of thioalkanoic acids **1** and **10** (0.01 mol/L) we observed a decrease in the concentration of CHP; the initial rate of CHP interaction with thiopropanoic acid **10** ($1 \cdot 10^{-3}$ M/s) turned out to be much higher than that for thioethanoic acid **1** ($7.5 \cdot 10^{-5}$ M/s). In addition, thioethanoic acid **1** interacted with CHP in the molar ratio of 1 : 1, while thiopropanoic acid **10** – in the ratio of 1 : 2, which was the evidence of deeper oxidation of its sulphide group.

Thus, lower antioxidant activity of thioethanoic acid **1** in comparison with homologous compound **10** in the autooxidation of methyl oleate is most probably connected with its lower antiperoxide activity. The latter is due to the effect of the carboxyl group on the electron density of sulphur atom. According to the data reported in [17, 18], the interaction of sulphides with hydroperoxides starts with electron transfer from sulphur atom to hydroperoxide. Correspondingly, a decrease of electron density at sulphur atom under the effect of electron-acceptor substituents must cause a decrease of the antiperoxide activity of sulphide group.

CONCLUSION

As the results of studies show, among ω-[3-(4-hydroxyaryl)propylthio]alkanoic acids synthesized by us, the most efficient inhibitors of the autooxidation of lipid substrates are *o*-di-*tert*-butyl-substituted compounds.

ω-[3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propylthio]alkanoic acids exceed known bioantioxidant phenosan in the antioxidant action because of the antiperoxide activity of sulphide groups; they are promising for further investigation as the inhibitors of free radical processes in biological systems.

REFERENCES

1 Menshchikova E. B., Zenkov N. K., Lankin V. Z., Bondar I. A., Trufanin V. A., Okislitelny Stress: Patologicheskiye Sostoyaniya i Zabolevaniya, ARTA, Novosibirsk, 2008.
2 Erokhin V. N., Krementsova A. V., Semenov V. A., Burlakova E. B., *Izv. RAN. Ser. Biol.*, 5 (2007) 583.
3 Zhizhina G. P., Zavarykina T. M., Mil E. M., Burlakova E. B., *Rad. Biol. Radioekol.*, 47, 4 (2007) 414.
4 Mil E. M., Albantova A. A., Burlakova E. B., *Rad. Biol. Radioekol.*, 50, 1 (2010) 58.
5 Kondratenko S. N., Starodubtsev A. K., Belyakova G. A., *Khim.-Farm. Zh.*, 43, 11 (2009) 54.
6 Zenkov N. K., Menshchikova E. B., Kandalintseva N. V., Oleynik A. S., Prosenko A. E., Gusachenko O. N., Shklyaeva O. A., Vavilin V. A., Lyakhovich V. V., *Biokhim.*, 72, 6 (2007) 790.
7 Kemeleva E. A., Vasyunina V. A., Sinitsina O. I., Khomchenko A. S., Gross M. A., Kandalintseva N. V., Prosenko A. E., Nevinskiy G. A., *Bioorg. Khim.*, 34, 4 (2008) 558.
8 Plotnikov M. B., Prosenko A. E., Smolyakova V. I., Ivanov I. S., Chernysheva G. A., Kandalintseva N. V., *Khim.-Farm. Zh.*, 44, 3 (2010) 65.
9 Oleynik A. S., Kuprina T. S., Pevneva N. Yu., Markov A. F., Kandalintseva N. V., Prosenko A. E., Grigoriev I. A., *Izv. RAN. Ser. Khim.*, 6 (2007) 1094.
10 Prosenko A. E., Markov A. F., Khomchenko A. S., Boyko M. A., Terakh E. I., Kandalintseva N. V., *Neftekhim.*, 6, 46 (2006) 442.
11 Author's Certification No. 1074865 USSR, 1983.
12 Prosenko A. E., Terakh E. I., Kandalintseva N. V., Pinko P. I., Gorokh E. A., Tolstikov G. A., *Zh. Prikl. Khim.*, 11 (2001) 1839.

13 Lyaskovskaya Yu. N., Piulskaya V. I., Metody Issledovaniya Okislitelnoy Porchi Zhirov, GOSINTI, Moscow, 1960.
14 Pat. No. 4.021.468 USA, 1977.
15 Roginskiy V. A., Fenolnye Antioksidanty: Reaktsionnaya Sposobnost' i Effektivnost', Nauka, Moscow, 1988.
16 Terakh E. I., Kandalintseva N. V., Nikulina V. V., Pinko P. I., Prosenko A. E., *Neftekhim.*, 3, 43 (2004) 237.
17 Pobedimskiy D. G., Buchachenko A. L., *Izv. AN SSSR. Ser. Khim.*, 6 (1968) 1181.
18 Pobedimskiy D. G., Buchachenko A. L., *Izv. AN SSSR. Ser. Khim.*, 6 (1968) 2720.