Synthesis and antioxidant properties of sodium *S*-[3-(hydroxyaryl)propyl] thiosulfates and [3-(hydroxyaryl)propane]-1-sulfonates*

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Sodium *S*-[3-(hydroxyaryl)propyl] thiosulfates and [3-(hydroxyaryl)propane]-1-sulfonates with various spatial hindrance of their phenolic OH groups were synthesized from dialkylphenols *via* a number of intermediate products. On a model reaction of oxidation of methyl oleate in aqueous sodium dodecyl sulfate, the rate constants of the interaction of the synthesized compounds with lipoperoxide radicals were determined.

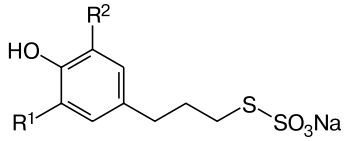
Key words: phenols, thiosulfates, sulfonates, antioxidants, free radicals, the Bunte salts.

A creation of hydrophilic "hybrid" compounds with several antioxidant-active centers in the molecule, which can inhibit a peroxidation of lipids in different ways, is one of the priorities in a search of new antioxidants to be used in biology and medicine. Derivatives of spatially hindered phenols, in which *para*-substituent contains alkylammonium,[1—4] isothiuronium,[3,4] and thiosulfate[4,5] groups, are among such compounds. In particular, it was earlier shown that sodium *S*-[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propyl] thiosulfate (**1a**) is characterized by a high antioxidant activity due to a concerted action of the phenol and thiosulfate groups[5] and shows hepatoprotecting,[4] cardioprotecting,[6] and immunomodulating[7] activities.

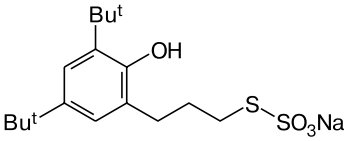
The present work is aimed on the synthesis of structural analogs of compound **1a**, *viz.*, thiosulfates **1** and sulfonates **2**, and on the comparative study of their antiradical activity.

Compounds **1** and **2** were obtained from 2,6-dialkylphenols *via* the intermediate transformation of the latter to (3-hydroxypropyl)phenols and halogen derivatives **3a—i** and **4a—i**, respectively.

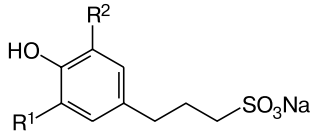
According to the known method,[8] alkylation of 2,6-di-*tert*-butylphenol with allyl alcohol in the presence of NaOH gave alcohol **3a**, which upon treatment with PBr_3 was converted to bromide **4a**,[9] upon treatment with HBr, to bromide **4d**, and by thermolysis, to alcohol **3g**.[10] Treatment of the latter with PBr_3 led to bromide **4g** (Scheme 1).



1a—h



1i



2a—h

$R^1 = R^2 = Bu^t$ (**a**); $R^1 = R^2 = cyclo\text{-}C_6H_{11}$ (**b**); $R^1 = R^2 = Me$ (**c**); $R^1 = R^2 = H$ (**d**); $R^1 = Me$, $R^2 = Bu^t$ (**e**); $R^1 = Me$, $R^2 = cyclo\text{-}C_6H_{11}$ (**f**); $R^1 = H$, $R^2 = Bu^t$ (**g**); $R^1 = H$, $R^2 = cyclo\text{-}C_6H_{11}$ (**h**)

In contrast to 2,6-di-*tert*-butylphenol, its less hindered analogs react with allyl alcohol not that straightforward: a remarkable amount of by-products is formed, resulting

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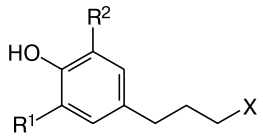
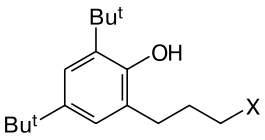


3a—h, 4a—h



3i, 4i

X = OH (**3a—i**), Br (**4a—h**), Cl (**4i**)

$R^1 = R^2 = Bu^t$ (**a**); $R^1 = R^2 =$ *cyclo*-C_6H_{11} (**b**); $R^1 = R^2 =$ Me (**c**); $R^1 = R^2 =$ H (**d**); $R^1 =$ Me, $R^2 = Bu^t$ (**e**); $R^1 =$ Me, $R^2 =$ *cyclo*-C_6H_{11} (**f**); $R^1 =$ H, $R^2 = Bu^t$ (**g**); $R^1 =$ H, $R^2 =$ *cyclo*-C_6H_{11} (**h**)

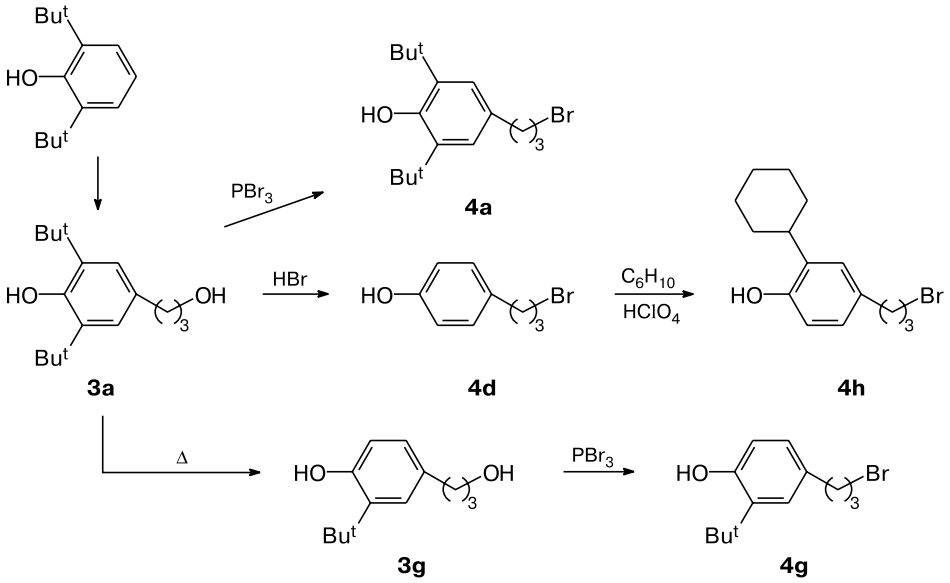
in a decrease of the target alcohols yields. In this connection, the less hindered bromopropyl-substituted phenols were obtained *via* the intermediate conversion of 2,6-dialkylphenols to their allyl derivatives **5** and **6** (Scheme 2).

Chloride **4i** was similarly synthesized from 2,4-di-*tert*-butylphenol (Scheme 3).

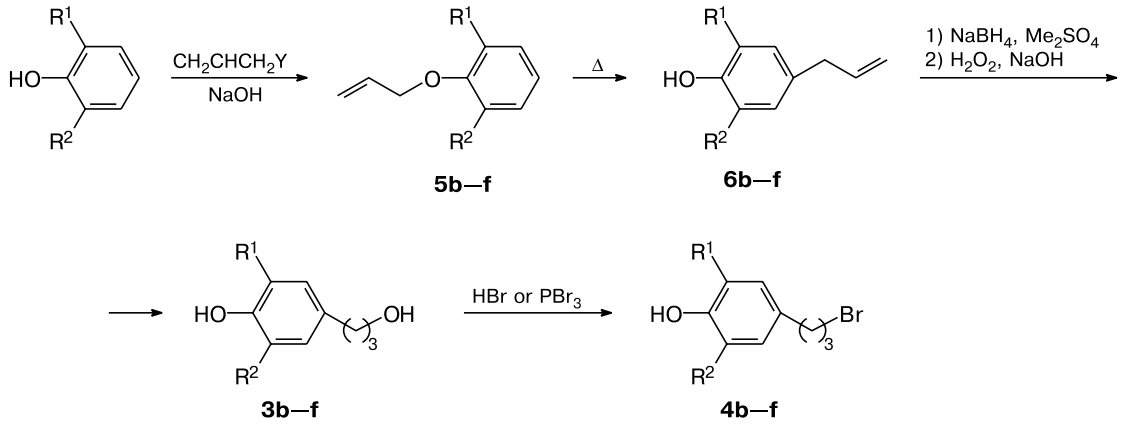
The final transformation of 3-arylpropylhalides **4** to thiosulfates **1** or sulfonates **2** was carried out by treatment with $Na_2S_2O_3$ or Na_2SO_3, respectively (Scheme 4).

Looking forward on practical utilization of synthesized compounds **1** and **2** (the inhibition of peroxidation of lipids in biological subjects), their antiradical activity in a model oxidation of methyl oleate in aqueous sodium dodecyl sulfate (SDS) was studied. This reaction can be considered as a particular case of the unsaturated fatty acid esters oxidation in aqueous solutions of surface-ac-

Scheme 1



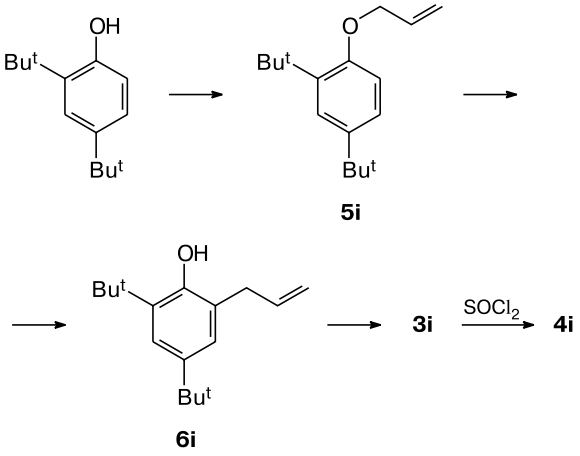
Scheme 2



Y = Cl, Br

$R^1 = R^2 =$ *cyclo*-C_6H_{11} (**b**); $R^1 = R^2 =$ Me (**c**); $R^1 = R^2 =$ H (**d**); $R^1 =$ Me, $R^2 = Bu^t$ (**e**); $R^1 =$ Me, $R^2 =$ *cyclo*-C_6H_{11} (**f**)

Scheme 3



tive compounds, which serves as a satisfactory model of the oxidation of lipids in biomembranes.[11]

The oxidation of methyl oleate (RH) in aq. SDS in the presence of 2,2′-azobis(2-methylpropionamidine) dihydrochloride (APH) as the initiator proceeds as a free-radical chain process and can be described as the following kinetic scheme:

$$APH \longrightarrow r^{\bullet} \longrightarrow R^{\bullet},$$

$$R^{\bullet} + O_2 \longrightarrow RO_2^{\bullet},$$

$$RO_2^{\bullet} + RH \xrightarrow{k_1} ROOH + R^{\bullet}, \quad (1)$$

$$RO_2^{\bullet} \longrightarrow \text{Molecular products}, \quad (2)$$

$$ArOH + RO_2^{\bullet} \xrightarrow{k_3} ROOH + ArO^{\bullet}, \quad (3)$$

$$RO_2^{\bullet} + ArO^{\bullet} \longrightarrow \text{Molecular products},$$

where $r^{\bullet}$ is a radical of the initiator, $R^{\bullet}$ and $RO_2^{\bullet}$ are alkyl and alkylperoxide radicals of methyl oleate, respectively, ArOH and $ArO^{\bullet}$ are a molecule and a radical of the inhibitor.

The difference between this scheme and the classic one, which describes an oxidation of hydrocarbons in homogeneous solutions, consists in the linear termination step in accordance with reaction (2).[11,12] This is confirmed by the fact that the rate of the uninhibited oxidation (W_0) is proportional to the rate of initiation (W_i)

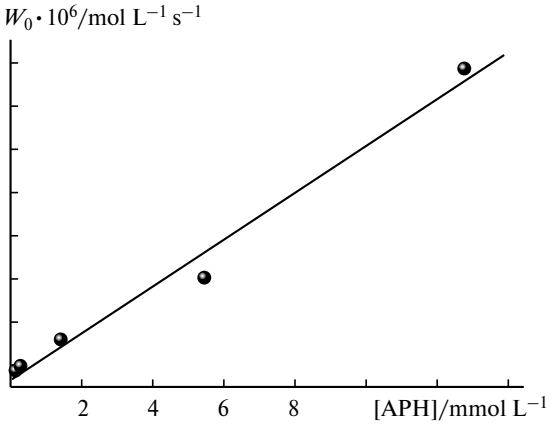


Fig. 1. The rate of the uninhibited oxidation of methyl oleate (W_0) in aq. SDS at 60 °C *vs.* concentration of the initiator (APH).

(Fig. 1). Earlier,[11] the similar phenomenon was found for the kinetics of oxidation of methyl oleate in aq. micellar solution of SDS.

A solution of the system of differential equations, corresponding to the kinetic scheme presented above, with the quasi-stationary approximation for all the radicals and with regard for the relation $W_0 = k_1[RH]W_i/k_2$ leads to the following expression:

$$W_0/W = 1 + 2k_3W_0[ArOH]/(k_1[RH]W_i),$$

where W is the rate of inhibited oxidation, [RH] is the concentration of the substrate in a sample, [ArOH] is the concentration of the inhibitor, k_1—k_3 are the rate constants of the corresponding reactions.

The relation k_3/k_1, which characterizes the reactivity of the synthesized compounds with respect to the peroxo radicals of methyl oleate, was found from the given equation with the use of experimentally determined values of W_0 and W. The k_3/k_1 values, averaged from several experiments (3—8), are given in Table 1. In all the cases, the average square error of the measurement did not exceed 25%.

The k_1 value derived during the oxidation of methyl oleate in aq. SDS at 60 °C and necessary for the calculation of the absolute values of k_3, is not reported in the literature. At the same time, it is known[12] that the k_3 value only slightly depends on the $RO_2^{\bullet}$ nature. This allowed us to estimate the k_1 value on the basis of the k_3 value,

Scheme 4

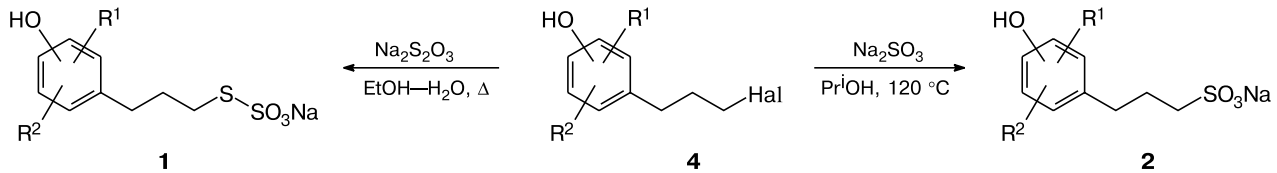


Table 1. Parameters of antiradical activity of compounds **1a,b,d—i** and **2a,c,h**

Compound	k_3/k_1	$k_3 \cdot 10^{-3}$ /L mol^{-1} s^{-1}
1a	270	5.6
1b	608	12.6
1d	9.2	0.19
1e	495	10.2
1f	736	15.2
1g	83	1.7
1h	95	2.0
1i	350	7.2
2a	168	3.5
2c	150	3.1
2h	88	1.8

determined for 2,6-di-*tert*-butyl-4-methylphenol (ionol) in the oxidation of methyl oleate in aq. SDS ($1.9 \cdot 10^4$ L mol^{-1} s^{-1} at 40 °C).[11] According to the known data,[12] the activation energy for the reaction of ionol with peroxide radicals is equal to ~4.5 kcal mol^{-1}, then for the case of 60 °C from the Arrhenius equation it follows that $k_3 = 2.9 \cdot 10^4$ L mol^{-1} s^{-1}. In the used by us model systems, the k_3/k_1 parameter for ionol is equal to 1400, consequently, $k_1 = 20.7$ L mol^{-1} s^{-1}. The k_3 values for compounds **1** and **2** were calculated based on this parameter.

The data obtained (see Table 1) show that in the oxidation of methyl oleate in aq. SDS, the synthesized compounds considerably differ in their reactivity toward active radicals: the describing them k_3 values range between 190 and $1.5 \cdot 10^4$ L mol^{-1} s^{-1}.

In the series of *ortho*-disubstituted thiosulfates **1a**, **1e**, **1b**, **1f**, when going from di-*tert*-butyl derivative to methyl-*tert*-butyl and further to dicyclohexyl and methylcyclohexyl derivative, an increase of the k_3 values was observed, which obviously can be explained by the decrease of sterical hindrance for reaction (3) to occur. Apparently the same factor causes the difference in the reactivity of isomers **1a** and **1i**.

According to the known data,[12] in oxidation of the model hydrocarbons, 2,6-dimethyl- and mono-*o*-*tert*-butyl-substituted phenols surpass the corresponding 2,6-di-*tert*-butylphenols in their k_3 constant values. At the same time, in the model system under consideration, the k_3 values for mono-*ortho*-substituted phenols **1g,h** yield to those of their disubstituted analogs **1a,b** from 3.3 to 6.3 times, while 2,6-dimethylphenol **2c** is less effective than the corresponding 2,6-di-*tert*-butylphenol **2a**. Apparently a hydration of the phenol OH groups in compounds **1** and **2** is responsible for such results. The formation of hydrogen bonds, such as ArOH...OH_2, as well as the spatial separation of ArOH and $RO_2^{\bullet}$ (hydrophilic molecules of the antioxidant mainly are in aqueous medium, while lipophilic radicals $RO_2^{\bullet}$ are in the micelles, formed from methyl oleate and SDS molecules), undoubtedly should lead to a decrease of the k_3 constant value.

Naturally, the importance of these factors increases with a decrease of spatial hindrance of the phenol OH group, though they remain actual for the case of 2,6-di-*tert*-butylphenol derivatives, too. Earlier,[4] it was shown that ionol and compound **1a** and **2a** in homogeneous solution of methyl oleate in chlorobenzene are charachterized by close k_3 values, *viz.*, $(2.3—2.8) \cdot 10^4$ L mol^{-1} s^{-1}. This allows us to believe that the difference in the k_3 values, observed for ionol and salts **1a** and **2a** in the model system under consideration, is connected not to the influence of various *para*-substituents on the electron density of the aromatic ring, but rather involves the different localization of these compounds in aqueous micellar solution: ionol as lipophilic antioxidant, apparently, is inside the micelles, while hydrophilic derivatives **1a** and **2a** are in the aqueous media.

In general, the obtained results show that a number of the synthesized compounds (thiosulfate derivatives **1b,e,f,i**) surpass the prototype **1a** in their antiradical activity and as hydrophilic bioantioxidants are of interest for further study.

Experimental

2,6-Dimethyl-, 2,6-di-*tert*-butyl-, 2,4-di-*tert*-butyl-, and 6-*tert*-butyl-2-methylphenols (Merck), as well as 2,6-dicyclohexyl- and 2-methyl-6-cyclohexylphenols, prepared by alkylation of phenol and *o*-cresol with cyclohexene according to the Kolka[13] method, were used as the starting materials for the synthesis of compounds **1** and **2**.

^{1}H NMR spectra of salts **1** and **2** were recorded on a Bruker DRX-500 spectrometer (500.13 MHz) in D_2O ($SiMe_4$ as the standard), of all the other compounds, in $CDCl_3$ ($CHCl_3$ as the standard). The melting points were determined in the capillary tubes with a PTP apparatus or with the Kofler heating table.

Sodium *S*-[3-(3,5-dicyclohexyl-4-hydroxyphenyl)propyl] thiosulfate (1b). A solution of $Na_2S_2O_3 \cdot 5H_2O$ (9.2 g, 37 mmol) in water (15 mL) was added to bromopropane **4b** (11.4 g, 30 mmol) in ethanol (30 mL), the mixture was refluxed for 6 h under argon, then cooled down and extracted with Et_2O. The extract was dried with Na_2SO_4 and the solvent was evaporated. The residue was washed with warm (~40 °C) hexane to give the target thiosulfate **1b** (10.7 g, 82%).

Sodium [3-(3,5-dicyclohexyl-4-hydroxyphenyl)propane]-1-sulfonate (2b). Bromopropane **4b** (5.7 g, 15 mmol), Na_2SO_3 (2.8 g, 22 mmol), propan-2-ol (15 mL), and water (15 mL) were placed into a 50-mL tube. The tube was sealed, placed into a thermostat, equipped with a shaking device, and kept for 5 h at 120 °C. After cooling down, the tube was opened, the organic phase was separated, the solvent was evaporated, the residue was washed with warm (~40 °C) hexane and then treated with acetone under heating (~50 °C). The undissolved in hot acetone residue was filtered off, the filtrate was concentrated to give sulfonate **2b** (3.1 g, 51%).

Sodium *S*-[3-(3,5-dimethyl-4-hydroxyphenyl)propyl] thiosulfate (1c), ***S*-[3-(5-*tert*-butyl-4-hydroxy-3-methylphenyl)propyl] thiosulfate (1e)**, ***S*-[3-(5-cyclohexyl-4-hydroxy-3-methylphenyl)propyl] thiosulfate (1f)**, ***S*-[3-(3-cyclohexyl-4-hydroxyphenyl)propyl] thiosulfate (1h)**, ***S*-[3-(3,5-di-*tert*-butyl-2-hydroxyphenyl)propyl] thiosulfate (1i)**, **[3-(4-hydroxy-3,5-dimethylphenyl)propane]-1-sulfonate (2c)**, **[3-(5-*tert*-butyl-4-hydroxy-3-methylphenyl)propane]-1-sulfonate (2e)** and **[3-(3-cyclohexyl-4-hydroxyphenyl)propane]-1-sulfonate (2h)** were obtained similarly. The syntheses of thiosulfates **1a,d,g** and sulfonates **2a,d,g** were described earlier.[5]

4-(3-Bromoprop-1-yl)-2,6-dicyclohexylphenol (4b). A mixture of alcohol **3b** (20 g, 63.2 mmol) and 40.5% aq. HBr (55 mL, 0.38 mol) was refluxed for 8 h with distillation of azeotrope, then it was cooled down and extracted with toluene (3×(10—15) mL). The extract was washed with water, dried with Na_2SO_4, the solvent was evaporated. The residue was distilled *in vacuo* to obtain bromo derivative **4b** (16.9 g, 70%).

4-(3-Bromoprop-1-yl)-2-*tert*-butyl-6-methylphenol (4e). Alcohol **3e** (8.5 g, 38 mmol) and DMF (3.6 mL, 46 mmol) were dissolved in toluene (40 mL), then PBr_3 (2 mL, 21 mmol) was added dropwise at 40—50 °C and the mixture was stirred for 2 h at 80 °C. Then the reaction mixture was cooled down to 60 °C, water (10 mL) was added and this was heated with stirring for 0.5 h at 80 °C. Then it was cooled down and extracted with toluene. The extract was washed with water, dried with Na_2SO_4, the solvent was evaporated. The residue was recrystallized from light petroleum to give bromo derivative **4e** (8.4 g, 77%).

Bromo derivatives **4c,f**, were obtained similarly by the reaction of alcohols **3c,f** with HBr, bromo derivative **4d**, by the reaction of alcohol **3a** with HBr. Bromides **4a,g** were obtained similarly to **4e**.

4-(3-Bromoprop-1-yl)-2-cyclohexylphenol (4h). Cyclohexene (12.8 mL, 126 mmol) was added dropwise to a mixture of 4-(3-bromoprop-1-yl)phenol **4d** (53.8 g, 0.25 mol) and 57% aq. perchloric acid (6 mL, 51 mmol of $HClO_4$) at 120 °C and this was stirred for 15 min. Then water (200 mL), benzene (100 mL), and 10% aq. NaOH (50 mL) were sequentially added; after thorough stirring, the organic and water phases were separated. The organic extract was washed with 10% aq. NaOH (2×50 mL), then neutralized with HCl, washed with water, dried with Na_2SO_4, the solvent was evaporated. The residue was distilled *in vacuo* to give compound **4h** (37.2 g, 50%).

1-Allyloxy-2,4-di-*tert*-butylbenzene (5i). 2,4-Di-*tert*-butylphenol (50 g, 0.24 mol) and NaOH (19.2 g, 0.48 mol) were dissolved in DMF (200 mL) under an inert gas atmosphere, then 3-chloroprop-1-ene (78 mL, 0.96 mol) was added dropwise and this was stirred for 4 h at 50 °C. The reaction mixture was cooled down and extracted with benzene. The extract was washed with water, dried with Na_2SO_4, the solvent was evaporated. The residue was distilled *in vacuo* to give ether **5i** (57.4 g, 96%).

2-Allyl-4,6-di-*tert*-butylphenol (6i). Allyloxybenzene **5i** (57.4 g, 0.23 mol) was kept for 3 h at 220—230 °C under an inert gas atmosphere, then it was distilled *in vacuo* to give allylphenol **6i** (52.2 g, 91%).

3-(3,5-Di-*tert*-butyl-2-hydroxyphenyl)propan-1-ol (3i). Dimethyl sulfate (6 mL, 62 mmol) was added dropwise to a suspension of allylphenol **6i** (15.3 g, 62 mmol) and $NaBH_4$ (2.81 g, 74.4 mmol) in THF (85 mL). After stiring for 0.5 h and cooling down to 3—5 °C, water (24 mL) was added dropwise to this. The mixture was heated up to 20 °C and 3 *M* aq. NaOH (22 mL, 66 mmol of NaOH) and 30% aq. H_2O_2 (23.5 mL, 0.23 mol of H_2O_2) were added dropwise, this was stirred for 0.5 h at 20 °C, neutralized with hydrochloric acid and extracted with toluene. The extract was washed with water, dried with Na_2SO_4, the solvent was evaporated. The residue was recrystallized from light petroleum to give alcohol **3i** (10.5 g, 64%).

Allyloxybenzenes **5b,c,e,f**, allylphenols **6b,c,e,f**, and alcohols **3b,c,e,f** were obtained similarly.

6-(3-Chloroprop-1-yl)-2,4-di(*tert*-butyl)phenol (4i). Thionyl chloride (3.3 mL, 45.9 mmol) was added dropwise to a mixture of alcohol **3i** (10 g, 37.8 mmol) and DMF (2.93 mL, 37.8 mmol) at 50—60 °C, this was heated up to 80 °C and stirred at this temperature for 3 h. After addition of water (20 mL) and benzene (50 mL), this was stirred for another 0.5 h at 70—80 °C. The organic layer was separated, washed with water, dried with Na_2SO_4, the solvent was evaporated. The residue was distilled *in vacuo* to give the target chloro derivative **4i** (7.4 g, 69%).

The structure and composition of the synthesized compounds were confirmed by elemental analysis and spectral data (Table 2).

Table 2. Yields, melting and boiling points, elemental analysis and ^{1}H NMR spectral data of compounds **1b,c,e,f,h,i**, **2b,c,e,h**, **3b,c,e,f,i**, **4b—i**, **5e,i**, and **6e,i**

Compound	Yield (%)	M.p. /°C	B.p./°C (1—2 Torr)	Found / Calculated (%)				Molecular formula	^{1}H NMR, δ (*J*/Hz)
				C	H	S	Hal		
1b	82	210	—	57.98 58.04	7.15 7.19	14.63 14.76	—	$C_{21}H_{31}NaO_4S_2$	1.05 (m, 2 H, *cyclo*-C_6H_{11}); 1.20 (m, 8 H, *cyclo*-C_6H_{11}); 1.52 (m, 2 H, *cyclo*-C_6H_{11}); 1.63 (m, 8 H, *cyclo*-C_6H_{11}); 1.93 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.51 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.67 (m, 2 H, *cyclo*-C_6H_{11}); 3.03 (t, 2 H, CH_2S, *J* = 8); 6.78 (s, 2 H, Ar)
1c	89	175	—	44.10 44.28	5.00 5.07	21.33 21.49	—	$C_{11}H_{15}NaO_4S_2$	1.92 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.12 (s, 6 H, Me); 2.52 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.98 (t, 2 H, CH_2S, *J* = 7); 6.84 (s, 2 H, Ar)

(*to be continued*)

Table 2 (*continued*)

Compound	Yield (%)	M.p. /°C	B.p./°C (1—2 Torr)	Found / Calculated (%) C	H	S	Hal	Molecular formula	^{1}H NMR, δ (*J*/Hz)
1e	76	170	—	49.24 49.39	6.13 6.22	18.73 18.84	—	$C_{14}H_{21}NaO_4S_2$	1.31 (s, 9 H, Bu^t); 1.94 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.17 (s, 3 H, Me); 2.53 (t, 2 H, $ArC\underline{H}_2$, *J* = 8); 3.02 (t, 2 H, CH_2S, *J* = 7); 6.88, 6.98 (both d, 1 H each, Ar, *J* = 1.5)
1f	89	150	—	52.33 52.44	6.25 6.33	17.43 17.50	—	$C_{16}H_{23}NaO_4S_2$	1.28 (m, 1 H, *cyclo*-C_6H_{11}); 1.41 (m, 4 H, *cyclo*-C_6H_{11}); 1.75 (m, 5 H + 2 H, *cyclo*-C_6H_{11}, $ArCH_2C\underline{H}_2$); 2.21 (s, 3 H, Me); 2.58 (t, 2 H, $ArC\underline{H}_2$, *J* = 8); 2.74 (m, 1 H, *cyclo*-C_6H_{11}); 3.13 (t, 2 H, CH_2S, *J* = 7); 6.78 (d, 1 H, Ar, *J* = 1.5); 6.84 (d, 1 H, Ar, *J* = 2)
1h	80	153	—	51.00 51.12	5.93 6.01	18.08 18.20	—	$C_{15}H_{21}NaO_4S_2$	1.15 (m, 1 H, *cyclo*-C_6H_{11}); 1.30 (m, 4 H, *cyclo*-C_6H_{11}); 1.66 (m, 5 H, *cyclo*-C_6H_{11}); 1.92 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.44 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.73 (m, 1 H, *cyclo*-C_6H_{11}); 2.74 (t, 2 H, CH_2S, *J* = 7); 6.79 (d, 1 H, Ar, *J* = 8.5); 6.89 (dd, 1 H, Ar, *J* = 8, *J* = 2.5); 7.00 (d, 1 H, Ar, *J* = 2)
1i	72	245	—	53.30 53.38	7.05 7.11	16.59 16.77	—	$C_{17}H_{27}NaO_4S_2$	1.28, 1.40 (both s, 9 H each, Bu^t); 2.09 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.78 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 3.21 (t, 2 H, CH_2S, *J* = 7.5); 7.11, 7.23 (both d, 1 H each, Ar, *J* = 2)
2b	51	290	—	62.49 62.66	7.60 7.76	7.90 7.97	—	$C_{21}H_{31}NaO_4S$	1.05 (m, 2 H, *cyclo*-C_6H_{11}); 1.20 (m, 8 H, *cyclo*-C_6H_{11}); 1.52 (m, 2 H, *cyclo*-C_6H_{11}); 1.58 (m, 8 H, *cyclo*-C_6H_{11}); 1.87 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.44 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.67 (m, 2 H, *cyclo*-C_6H_{11}); 2.74 (t, 2 H, CH_2S, *J* = 8); 6.78 (s, 2 H, Ar)
2c	80	222	—	49.50 49.62	6.55 5.68	11.87 12.04		$C_{11}H_{15}NaO_4S$	1.90 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.10 (s, 6 H, Me); 2.48 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.78 (t, 2 H, CH_2S, *J* = 7.5); 6.80 (s, 2 H, Ar)
2e	85	>300 (decomp.)	—	54.38 54.53	6.68 6.86	10.27 10.40	—	$C_{14}H_{21}NaO_4S$	1.45 (s, 9 H, Bu^t); 2.10 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.30 (s, 3 H, Me); 2.72 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.97 (t, 2 H, CH_2S, *J* = 8); 7.06, 7.17 (both d, 1 H each, Ar, *J* = 1.5)
2h	82	231	—	56.17 56.23	6.56 6.61	9.94 10.01	—	$C_{15}H_{21}NaO_4S$	1.11 (m, 1 H, *cyclo*-C_6H_{11}); 1.28 (m, 4 H, *cyclo*-C_6H_{11}); 1.66 (m, 5 H, *cyclo*-C_6H_{11}); 1.91 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.44 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.73 (m, 1 H, *cyclo*-C_6H_{11}); 2.74 (t, 2 H, CH_2S, *J* = 8); 6.79 (d, 1 H, Ar, *J* = 8); 6.89 (dd, 1 H, Ar, *J* = 8, *J* = 2); 7.00 (d, 1 H, Ar, *J* = 2)
3b	86	99—101	215—235	79.55 79.70	10.00 10.19	—	—	$C_{21}H_{32}O_2$	1.30 (m, 2 H, *cyclo*-C_6H_{11}); 1.45 (m, 8 H + 1 H, *cyclo*-C_6H_{11}, $CH_2O\underline{H}$); 1.81 (m, 10 H + 2 H, *cyclo*-C_6H_{11}, $ArCH_2C\underline{H}_2$); 2.57 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.69 (m, 2 H, *cyclo*-C_6H_{11}); 3.62 (t, 2 H, $C\underline{H}_2OH$, *J* = 8); 4.66 (s, 1 H, OH); 6.75 (s, 2 H, Ar)

(*to be continued*)

Table 2 (*continued*)

Compound	Yield (%)	M.p. /°C	B.p./°C (1—2 Torr)	Found / Calculated (%)				Molecular formula	^{1}H NMR, δ (*J*/Hz)
				C	H	S	Hal		
3c	57	66—67	—	73.15 73.30	8.88 8.95	—	—	$C_{11}H_{16}O_2$	1.50 (br.s, 1 H, $CH_2O\underline{H}$); 1.83 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.20 (s, 6 H, Me); 2.56 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 3.65 (t, 2 H, $C\underline{H}_2OH$, *J* = 7); 4.47 (br.s, 1 H, OH); 6.79 (s, 2 H, Ar)
3e	75	61—63	148—150	75.57 75.63	10.04 9.97	—	—	$C_{14}H_{22}O_2$	1.39 (s, 9 H, Bu^t); 1.43 (br.s, 1 H, $CH_2O\underline{H}$); 1.85 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.21 (s, 3 H, Me); 2.60 (t, 2 H, $ArC\underline{H}_2$, *J* = 8); 3.66 (t, 2 H, $C\underline{H}_2OH$, *J* = 6.5); 4.67 (s, 1 H, OH); 6.79 (d, 1 H, Ar, *J* = 2); 6.92 (d, 1 H, Ar, *J* = 2.5)
3f	83	71—72	130—140	77.29 77.38	9.65 9.74	—	—	$C_{16}H_{24}O_2$	1.28 (m, 1 H + 1 H, *cyclo*-C_6H_{11}, $CH_2O\underline{H}$); 1.41 (m, 4 H, *cyclo*-C_6H_{11}); 1.75 (m, 1 H, *cyclo*-C_6H_{11}); 1.84 (m, 4 H, *cyclo*-C_6H_{11}); 2.11 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.21 (s, 3 H, Me); 2.59 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.74 (m, 1 H, *cyclo*-C_6H_{11}); 3.65 (t, 2 H, $C\underline{H}_2OH$, *J* = 6.5); 4.52 (s, 1 H, OH); 6.77 (d, 1 H, Ar, *J* = 1.5); 6.84 (d, 1 H, Ar, *J* = 2)
3i	64	98—100	—	77.00 77.22	10.55 10.67	—	—	$C_{17}H_{28}O_2$	1.28, 1.41 (both s, 9 H each, Bu^t); 1.87 (m, 2 H, $ArCH_2C\underline{H}_2$); 1.88 (s, 1 H, $CH_2O\underline{H}$); 2.75 (t, 2 H, $ArC\underline{H}_2$, *J* = 7); 3.66 (t, 2 H, $C\underline{H}_2OH$, *J* = 6); 6.70 (s, 1 H, OH); 6.96, 7.17 (both d, 1 H each, Ar, *J* = 2.5)
4b	70	74—75	205—207	66.43 66.49	8.19 8.24	—	20.89 21.06	$C_{21}H_{31}BrO$	1.35 (m, 2 H, *cyclo*-C_6H_{11}); 1.45 (m, 8 H, *cyclo*-C_6H_{11}); 1.81 (m, 2 H, *cyclo*-C_6H_{11}); 1.89 (m, 8 H, *cyclo*-C_6H_{11}); 2.05 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.71 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 2.76 (m, 2 H, *cyclo*-C_6H_{11}); 3.37 (t, 2 H, CH_2Br, *J* = 7); 4.70 (s, 1 H, OH); 6.75 (s, 2 H, Ar)
4c	89	53—55	120—130	54.25 54.34	6.13 6.22	—	32.75 32.86	$C_{11}H_{15}BrO$	2.19 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.30 (s, 6 H, Me); 2.71 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 3.46 (t, 2 H, CH_2Br, *J* = 7); 4.68 (s, 1 H, OH); 6.87 (s, 2 H, Ar)
4d	91	38—40	121—124	50.33 50.26	5.21 5.15	—	36.97 37.15	$C_9H_{11}BrO$	2.11 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.70 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 3.37 (t, 2 H, CH_2Br, *J* = 7); 5.00 (s, 1 H, OH); 6.76, 7.14 (both d, 2 H each, Ar, *J* = 8)
4e	77	Tar	122—123	58.84 58.96	7.29 7.42	—	27.89 28.01	$C_{14}H_{21}BrO$	1.43 (s, 9 H, Bu^t); 2.05 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.23 (s, 3 H, Me); 2.68 (t, 2 H, $ArC\underline{H}_2$, *J* = 8); 3.40 (t, 2 H, CH_2Br, *J* = 6.5); 4.66 (s, 1 H, OH); 6.84 (d, 1 H, Ar, *J* = 1.5); 7.17 (d, 1 H, Ar, *J* = 2.5)
4f	76	43—44	170—175	61.60 61.74	7.31 7.45	—	25.52 25.67	$C_{16}H_{23}BrO$	1.28 (m, 1 H, *cyclo*-C_6H_{11}); 1.41 (m, 4 H, *cyclo*-C_6H_{11}); 1.75 (m, 1 H, *cyclo*-C_6H_{11}); 1.85 (m, 4 H, *cyclo*-C_6H_{11}); 2.10 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.21 (s, 3 H, Me); 2.64 (t, 2 H, $ArC\underline{H}_2$, *J* = 8); 2.74 (m, 1 H, *cyclo*-C_6H_{11}); 3.38 (t, 2 H, CH_2Br, *J* = 6.5); 4.49 (s, 1 H, OH); 6.77, 6.83 (both d, 1 H each, Ar, *J* = 2)

(*to be continued*)

Table 2 (*continued*)

Compound	Yield (%)	M.p. /°C	B.p./°C (1—2 Torr)	Found / Calculated (%)				Molecular formula	^{1}H NMR, δ (*J*/Hz)
				C	H	S	Hal		
4g	60	Tar	128—129	57.49 57.57	6.99 7.06	—	29.39 29.46	$C_{13}H_{19}BrO$	1.40 (s, 9 H, Bu^t); 2.00—2.06 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.68 (t, 2 H, $ArC\underline{H}_2$, *J* = 7.5); 3.35 (t, 2 H, CH_2Br, *J* = 6.5); 4.85 (s, 1 H, OH); 6.56 (d, 1 H, Ar, *J* = 8); 6.87 (dd, 1 H, Ar, *J* = 8, *J* = 2); 7.07 (d, 1 H, Ar, *J* = 2)
4h	50	Tar	202—207	60.70 60.61	7.23 7.12	—	26.75 26.88	$C_{15}H_{21}BrO$	1.30 (m, 1 H, *cyclo*-C_6H_{11}); 1.44 (m, 4 H, *cyclo*-C_6H_{11}); 1.78 (m, 1 H, *cyclo*-C_6H_{11}); 1.88 (m, 4 H, *cyclo*-C_6H_{11}); 2.14 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.71 (t, 2 H, $ArC\underline{H}_2$, *J* = 7); 2.83 (m, 1 H, *cyclo*-C_6H_{11}); 3.41 (t, 2 H, CH_2Br, *J* = 7); 4.97 (s, 1 H, OH); 6.69 (d, 1 H, Ar, *J* = 8); 6.89 (dd, 1 H, Ar, *J* = 8, *J* = 2); 7.03 (d, 1 H, Ar, *J* = 2)
4i	69	Tar	123—127	72.00 72.19	9.49 9.62	—	12.45 12.53	$C_{17}H_{27}ClO$	1.27, 1.42 (both s, 9 H each, Bu^t); 2.04 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.69 (t, 2 H, $ArC\underline{H}_2$, *J* = 7); 2.75 (t, 2 H, CH_2Cl, *J* = 6); 4.99 (br.s, 1 H, OH); 6.98, 7.17 (both d, 1 H each, Ar, *J* = 2.5)
5e	93	Tar	90—95	82.40 82.30	9.93 9.87	—	—	$C_{14}H_{20}O$	1.45 (s, 9 H, Bu^t); 2.25 (s, 3 H, Me); 4.26 (m, 2 H, OCH_2); 5.28, 5.49 (both m, 1 H each, $=CH_2$); 6.15 (m, 1 H, —CH=); 7.02 (m, 2 H, Ar); 7.10 (m, 1 H, Ar)
5i	96	Tar	103—107	82.91 82.87	10.68 10.64	—	—	$C_{17}H_{26}O$	1.41, 1.52 (both s, 9 H each, Bu^t); 4.61 (dt, 2 H, OCH_2, *J* = 5, *J* = 1.5); 5.33 (dm, 1 H, $=CH_2$, *J* = 5.5); 5.52 (dm, 1 H, $=CH_2$, *J* = 17.5); 6.14 (m, 1 H, —CH=); 6.82 (d, 1 H, Ar, *J* = 8.5); 7.19 (dd, 1 H, Ar, *J* = 8.5, *J* = 2.5); 7.37 (d, 1 H, Ar, *J* = 2.5)
6e	85	Tar	95—98	82.24 82.30	9.79 9.87	—	—	$C_{14}H_{20}O$	1.45 (s, 9 H, Bu^t); 2.25 (s, 3 H, Me); 4.27 (m, 2 H, $ArC\underline{H}_2$); 4.65 (s, 1 H, OH); 5.09 (m, 2 H, $=CH_2$); 5.99 (m, 1 H, —CH=); 7.05 (d, 1 H, Ar, *J* = 2); 7.13 (d, 1 H, Ar, *J* = 1.5)
6i	91	Tar	110—115	82.80 82.87	10.57 10.64	—	—	$C_{17}H_{26}O$	1.34, 1.46 (both s, 9 H each, Bu^t); 3.45 (dt, 2 H, $ArC\underline{H}_2$, *J* = 6.5, *J* = 1.5); 5.10 (s, 1 H, OH); 5.25—5.32 (m, 2 H, $=CH_2$); 6.03—6.11 (m, 1 H, —CH=); 6.99 (d, 1 H, Ar, *J* = 2.5); 7.17 (d, 1 H, Ar, *J* = 2)

The synthesis and physical and chemical characteristics of allyl derivatives **5b,c,f** [14] and **6b,c,f** [14] and bromopropane **4a** [9] were described earlier.

In the kinetic studies, a manometric method for the determination of the rate constant values for the reaction of phenols with peroxide radicals was used.[12] In this work, methyl oleate (Acros Organics) was used, oxidation of which was carried out at 60 °C in aq. SDS, containing dihydrate of tetrasodium salt of ethylenediaminetetraacetic acid (0.2 mmol L^{-1}); pH 7.37 (phosphate buffer, 50 mmol L^{-1}). APH (Acros Organics) was used as the initiator. The rate of oxidation was monitored using a high-sensitive capillary. A construction of kinetic curves and their mathematical treatment were carried out with Origin 6.0 program.

The working concentrations of components in a sample were as follows: methyl oleate, 0.133 mol L^{-1}; APH, 6.15 mmol L^{-1}; SDS, 0.25 mol L^{-1}. Compound **1** and **2** were added in amounts of $4.5 \cdot 10^{-5}$—$2.3 \cdot 10^{-4}$ mol L^{-1}. The rate of initiation W_i (determined by the method of inhibitors[12]) was $7 \cdot 10^{-8}$ mol L^{-1} s^{-1}, the length of oxidation chains was no less than 27 units.

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