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Synthesis and Antioxidative Activity
of S-Substituted 2-Mercapto-1,4-dihydroxybenzenes

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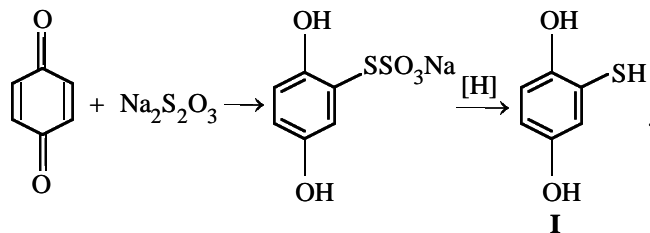
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Abstract—S-Substituted 2-mercapto-1,4-dihydroxybenzenes were prepared, and their antioxidative activity in autooxidation of cumene and in the reactions with cumylperoxy radicals and cumyl hydroperoxide was studied.

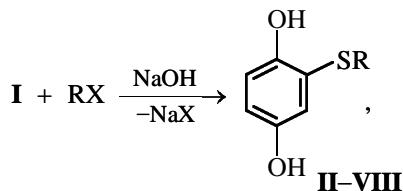
Sulfur-substituted phenols as effective oxidation inhibitors are widely used for stabilization of petroleum products [1]. Their high inhibiting performance is due to the presence in one molecule of two functional groups: phenolic hydroxyl and sulfide sulfur, making these compounds capable to inhibit oxidation by scavenging of peroxy radicals and decomposition of peroxides [2, 3].

Proceeding with studies on synthesis of phenolic sulfides [2–7], we prepared S-substituted 2-mercapto-1,4-dihydroxybenzenes and studied their antioxidative activity in cumene oxidation.

2-Mercapto-1,4-dihydroxybenzene **I** was prepared as follows:



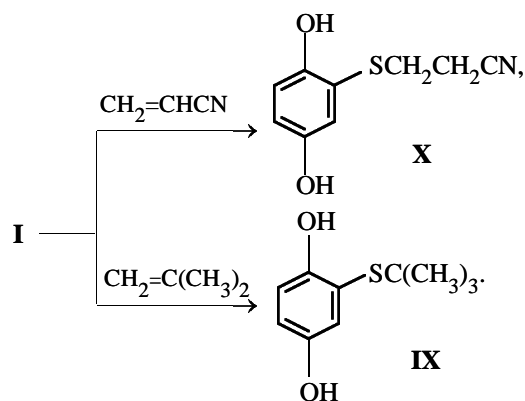
S-Methyl (**II**), S-ethyl (**III**), S-isopropyl (**IV**), S-carboxymethyl (**V**), S-acetyl (**VI**), S-allyl (**VII**), and S-benzyl (**VIII**) derivatives of **I** were prepared by the reactions of **I** with the corresponding halides in the presence of NaOH:



where R = CH₃, X = I (**II**); R = C₂H₅, X = Br (**III**);

R = (CH₃)₂CH, X = Br (**IV**); R = CH₂COOH, X = Cl (**V**); R = CH₃CO, X = Br (**VI**); R = CH₂=CHCH₂, X = Br (**VII**); R = C₆H₅CH₂, X = Cl (**VIII**).

S-*tert*-Butyl (**IX**) and S-(2-cyanoethyl) (**X**) derivatives of **I** were prepared, respectively, by addition of **I** to acrylonitrile in the presence of triethylamine and to 2-methylpropene in the presence of catalytic amounts of sulfuric acid:



The purity of the compounds was checked by TLC and elemental analysis (Table 1), and their structures were proved by IR and ¹H NMR spectroscopy.

The IR spectra of **I–X** contain absorption bands at about 1450 (C=C stretching vibrations in the aromatic ring), 3450 (stretching vibrations of the O–H bond involved in hydrogen bonding with the adjacent S atom [8]), and 810–860 cm⁻¹ (1,2,4-substituted benzene ring). The ¹H NMR spectra of mercaptophenols **I–X** contain a proton signal from two hydroxy groups (7.4 ppm). The multiplets of three benzene ring protons are observed at about 5.9 ppm. Compound **I** exhibits a band at 2530 cm⁻¹ in the IR spec-

Table 1. Yields, melting points, retention factors (R_f), and elemental analyses of **I–X**

Compound	mp, °C	Yield, %	R_f	Found, %			Formula	Calculated, %		
				C	H	S		C	H	S
I	117–117.5	38	0.57	50.83	4.07	22.36	C ₆ H ₆ O ₂ S	50.68	4.25	22.55
II	123–124	47	0.82	53.49	5.28	20.32	C ₇ H ₈ O ₂ S	53.82	5.16	20.51
III	135–136	35	0.63	56.21	5.75	20.66	C ₈ H ₁₀ O ₂ S	56.45	5.92	20.49
IV	142–143	42	0.47	57.83	5.62	17.23	C ₉ H ₁₂ O ₂ S	58.67	6.56	17.40
V	147–148	55	0.73	60.73	7.41	16.38	C ₁₀ H ₁₄ O ₂ S	60.57	7.12	16.17
VI	140–142	49	0.87	50.72	4.17	15.27	C ₉ H ₈ O ₂ S	50.94	3.79	15.11
VII	99–100	60	0.68	52.37	4.61	17.59	C ₈ H ₈ O ₃ S	52.16	4.38	17.41
VIII	132–133	26	0.85	59.12	5.74	17.39	C ₉ H ₁₀ O ₂ S	59.32	5.53	17.60
IX	97–98	75	0.57	55.52	4.19	16.58	C ₉ H ₉ NO ₂ S	55.37	4.65	16.42
X	148–149	36	0.90	67.43	5.39	13.67	C ₁₃ H ₁₂ O ₂ S	67.25	5.21	13.80

trum (S–H stretching vibrations), and its NMR spectrum contains an SH proton singlet at 3.3 ppm. The IR and ¹H NMR spectra of **II–X** exhibit features characteristic of the substituents at the S atom.

To evaluate the inhibiting activity of **I–X**, we used as model substrate cumene, as the mechanism of its oxidation is well understood. Experiments on cumene autooxidation in the presence of **I–X** revealed their fairly high inhibiting performance. Experiments on oxidation of cumene initiated with azobis(isobutyronitrile) (AIBN; 60°C, [AIBN] = 2 × 10⁻² M) showed that these compounds actively terminate oxidation chains, reacting with cumylperoxy radicals. Data for **I** as example are shown in Fig. 1. From the induction period τ_{ind} , we calculated the stoichiometric inhibition coefficient f equal to the number of oxidation chains

terminated on one molecule of an inhibitor and its transformation products:

$$f = \tau_{\text{ind}} v_{\text{ind}} / [\text{In}]_0,$$

where τ_{ind} is the induction period; v_{ind} , initiation rate; and $[\text{In}]_0$, initial concentration of inhibitor In.

From the kinetics of the oxygen uptake, we calculated the rate constants of the reactions of the inhibitors with peroxy radicals k_7 [8, 9]. To do this, we transformed the kinetic curves of the oxygen uptake from the coordinates $[\text{O}_2] - \tau$ to the coordinates $[\text{O}_2]^{-1} - \tau^{-1}$ and from the slope $\tan \alpha$, equal [9, 10] to

$$\tan \alpha = f k_7 [\text{In}]_0 / (k_2 [\text{RH}] v_{\text{ind}}),$$

found the constant k_7 :

$$k_7 = \tan \alpha k_2 [\text{RH}] v_{\text{ind}} / f [\text{In}]_0,$$

where k_2 is the rate constant of chain initiation [9, 10], equal to 1.51 l mol⁻¹ s⁻¹; $[\text{RH}] = 6.9$ M.

Table 2 shows that the constants k_7 for the compounds with electron-donor substituents are higher compared to the compounds with electron-acceptor substituents. As for f , it varies in the range 1.05–2.20.

Reactions of **I–X** with cumyl hydroperoxide (CHP) were performed in chlorobenzene under nitrogen at 110°C. All the compounds **I–X** decompose CHP. Figure 2 shows (by the example of **I**) that the kinetic curve of CHP decomposition in the presence of mercaptophenols is S-shaped, which is typical of autocatalytic processes. The reaction starts with a certain induction period in which the consumption of CHP is insignificant; this is followed by fast catalytic decom-

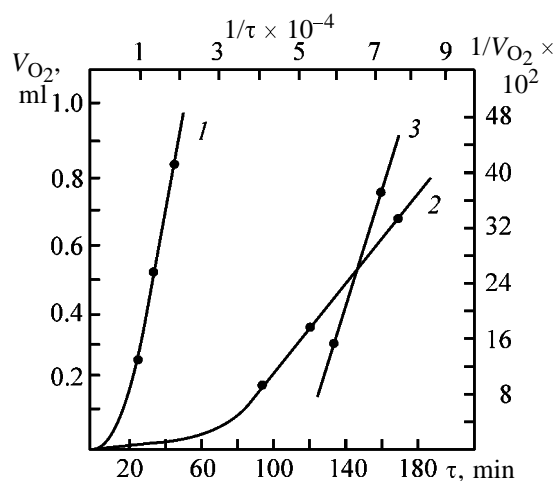


Fig. 1. Kinetic curves of O₂ uptake in initiated oxidation of cumene (1) without additives and (2) in the presence of **I**. (3) Linearization of curve 2 in the coordinates $1/\tau - 1/V_{\text{O}_2}$. (V_{O_2}) Volume of oxygen taken up and (τ) time.

position of CHP and then by reaction deceleration due to a decrease in the CHP concentration. Apparently, the inhibitor first reacts with CHP to give a product that catalytically decomposes CHP.

To determine the reaction order, we studied how the initial rate of the catalytic decomposition of CHP depends on the concentrations of the reactants. We found that the initial rate v_0 of catalytic decomposition of CHP under the action of **I–X** obeys the kinetic equation

$$v_0 = k[\text{In}][\text{ROOH}]^2.$$

To determine the reaction stoichiometry, we took CHP in excess. The catalytic factor ν characterizes the number of CHP molecules decomposed with one inhibitor molecule; it was calculated by the formula

$$\nu = [\text{ROOH}]_0 - [\text{ROOH}]_\infty / [\text{In}]_0,$$

where $[\text{ROOH}]_0$ and $[\text{ROOH}]_\infty$ are, respectively, the initial and final concentrations of [CHP], and $[\text{In}]_0$ is the initial inhibitor concentration.

Experiments showed that one molecule of **I–X** can decompose up to several thousands of CHP molecules (Table 2). The kinetic parameters of the reaction show certain correlation with the properties of substituents at the S atom. In particular, in going to branched alkyl substituents (compounds **II–V**) k decreases, probably owing to steric factors; ν is higher for the compounds with electron-donor substituents at the S atom.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75-IR spectrophotometer, and the ^1H NMR spectra, on a Varian T-60 spectrometer, with tetramethylsilane as internal reference.

2-Mercapto-1,4-dihydroxybenzene I. A solution of 43.2 g of benzoquinone in 150 ml of glacial acetic acid was heated to 40–50°C, and then a solution of 150 g of $\text{Na}_2\text{S}_2\text{O}_3$ in 200 g of water was gradually added, avoiding warming-up of the reaction mixture by more than 10°C. After short stirring, the transparent and almost colorless solution was saturated with KCl to precipitate sodium *S*-(2,5-dihydroxyphenyl) thiosulfate. A solution of 2.6 g of this salt in 10 ml of water was mixed with 20 ml of concentrated HCl, and 5 g of zinc dust was gradually added; the reaction temperature was maintained at 40–50°C until the gas evolution ceased.

Table 2. Kinetic parameters of the reactions of mercaptophenols **I–X** with cumylperoxy radicals k_7 and f (60°C, $[\text{AIBN}] = 2 \times 10^{-2}$ M) and of decomposition of cumyl hydroperoxide k and ν (110°C)

Compound	$k_7 \times 10^{-4}$, $1 \text{ mol}^{-1} \text{ s}^{-1}$	f	k , $1 \text{ mol}^{-1} \text{ s}^{-1}$	ν
I	2.15	1.27	10.45	4500
II	1.53	2.20	3.24	3350
III	1.71	2.11	2.45	2730
IV	2.70	1.92	1.96	1840
V	1.52	1.05	1.62	400
VI	2.17	1.72	2.99	2800
VII	1.05	1.64	3.50	1770
VIII	1.41	1.57	3.10	1050
IX	1.25	1.62	4.63	1500
X	1.15	1.74	4.67	2870

2,5-Dihydroxyphenyl methyl sulfide II. A 2-g portion of NaOH was added at 10–15°C to a solution of 7.1 g (0.05 mol) of **I** in 30 ml of isopropyl alcohol, after which 7.1 g of methyl iodide was added at the same temperature. The reaction was performed under nitrogen. The temperature was raised to 60°C, after which the mixture was stirred for an additional 3 h and washed first with 2 M HCl and then with water to neutral reaction. The organic layer was treated with petroleum ether (30–60°C) and dried over sodium sulfate.

Compounds **III**, **IV**, **VII**, **VIII**, and **X** were prepared similarly.

2,5-Dihydroxyphenyl tert-butyl sulfide IX. A 3-ml portion of isobutylene was added to a mixture of 7.1 g of **I** and five drops of concentrated H_2SO_4 saturated with $(\text{NH}_4)_2\text{SO}_4$, heated to 110–120°C. Then the mixture was neutralized with 13 ml of 2 M NaOH, treated with petroleum ether, and washed three

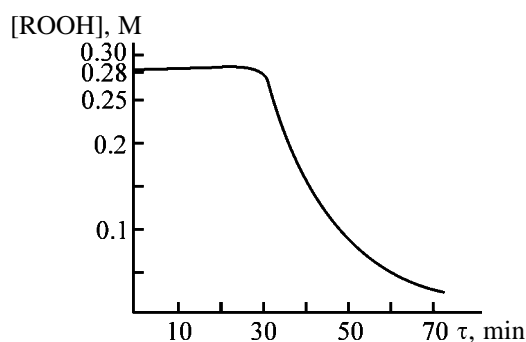


Fig. 2. Kinetic parameters of decomposition of cumyl hydroperoxide (ROOH) under the action of **I**. $[\text{In}] = 3 \times 10^{-4}$, $[\text{ROOH}]_0 = 0.285$ M. (τ) Time.

times with water. After drying over Na₂SO₄, the solvent was distilled off.

2,5-Dihydroxyphenyl 2-carboxymethyl sulfide V.

A 7.1-g portion of **I** was added to a solution of 2 g of NaOH in 10 ml of water, and a concentrated solution of 4.7 g of chloroacetic acid, neutralized with sodium hydrogen carbonate, was added with stirring and cooling. After 5 h, the solution was heated, impurities were steam-distilled, and the solution was acidified with dilute H₂SO₄.

2,5-Dihydroxyphenyl 2-cyanoethyl sulfide X.

A mixture of 7.1 g of **I**, 20 ml of anhydrous benzene, and a drop of triethylamine was stirred at 60–70°C for 3 h. Then the mixture was washed with water and dried over Na₂SO₄. The solvent was distilled off, and the product was recrystallized from diethyl ether.

CONCLUSIONS

(1) 2-Mercapto-1,4-dihydroxybenzene was prepared and converted into various S-substituted derivatives.

(2) The compounds synthesized exhibit synergism as inhibitors of cumene oxidation and, being polyfunctional antioxidants, terminate cumene oxidation chains by reactions with peroxy radicals and catalytically decompose cumene hydroperoxide.

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