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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Synthesis and Antioxidant Activity of 1-Amino-4-phenyl-2-butanethiols

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Abstract—1-Amino-4-phenyl-2-butanethiols were synthesized and characterized and their antioxidant activity in auto-oxidation of cumene and in their reaction with cumyl peroxide radicals and cumyl hydroperoxide was studied.

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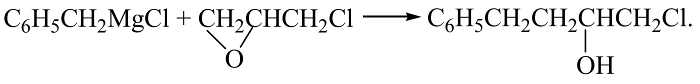
A topical task of modern tribochemistry is to improve the stability of petroleum fuels and oils against oxidation in prolonged storage and service. The only way to stabilize fuels and oils is to add antioxidant additives. At present, various alkyl derivatives of phenols, aromatic amines, aminophenols, various sulfides, and metal salts of dithio-phosphoric acids are widely used as antioxidant additives [1].

Published data on the use of 1,2-aminothiols as inhibitors of oxidation of fuels and other petroleum products are scarce. There have been separate reports that, owing to their antioxidant properties, aminothiols and amino sulfides can be used to stabilize polymethacrylic acid under the action of X-rays [2]. Some aminothiols are used as inhibitors of oxidation and decomposition of organic peroxides and stabilizers of fats and fat-containing products [3].

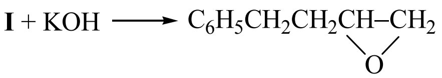
In this study, we synthesized 1-amino-4-phenyl-2-propanethiol and examined the relationship between its structure and antioxidant activity. As the starting product served 1-chloro-4-phenyl-2-butanol (**I**) synthesized by reacting benzylmagnesium chloride with epichlorohydrin:



$$C_6H_5CH_2MgCl + \underset{\diagdown O \diagup}{CH_2CH}CH_2Cl \longrightarrow C_6H_5CH_2CH_2\underset{OH}{\underset{|}{CH}}CH_2Cl.$$

The highest yield of 1-chloro-4-phenyl-2-butanol (**I**) is obtained at a 1 : 2 ratio between the Grignard reagent and epichlorohydrin. At a 1 : 1 molar ratio, the yield of the target product sharply decreases. The physicochemical constants of 1-chloro-4-phenyl-2-butanol are consistent with published data [4].

Finely ground potassium hydroxide in a solution of anhydrous ether was used to dehydrochlorinate 1,2-chlorohydrin **I** and convert it to the corresponding 1,2-epoxy-4-phenylbutane (**II**):



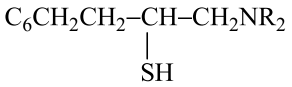
$$\mathbf{I} + KOH \longrightarrow C_6H_5CH_2CH_2\underset{\diagdown O \diagup}{CH{-}CH_2}$$

II

The physicochemical constants of oxirane **II** we synthesized are consistent with published data [5].

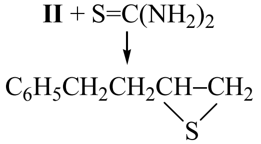
1,2-Epithio-4-phenylbutane (**III**) was synthesized by anionotropic substitution of the oxygen atom in oxirane **II** with a sulfur atom from the thiocarbamide molecule in the presence of sulfuric acid:

Table 1. Selected physicochemical parameters of 1,2-aminobutanethiols **IV–IX**



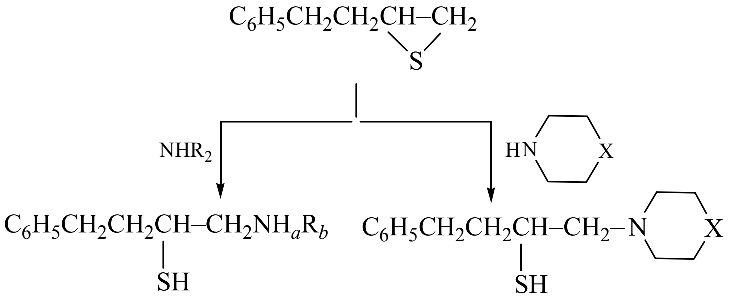
$$C_6CH_2CH_2\text{–}\underset{\displaystyle SH}{\underset{|}{CH}}\text{–}CH_2NR_2$$

Comp. no.	Yield, %	bp., (*p*, mm Hg)	n_D^{20}	R	C	H	N	S
					found, %/calculated,%			
IV	65	110(1)	1.5217	0.49	70.70/70.89	9.54/9.70	5.76/5.91	13.32/13.50
V	67	102(1)	1.5240	0.57	69.20/69.39	10.03/10.22	6.04/6.22	14.05/14.22
VI	70	120(1)	1.5317	0.68	70.12/70.29	10.31/10.46	5.73/5.86	13.20/13.39
VII	69	112(0.8)	1.5485	0.47	72.13/72.29	9.09/9.24	5.49/5.62	12.69/12.85
VIII	75	149(0.4)	1.5618	0.55	71.33/71.49	8.79/8.94	5.81/5.96	13.42/13.62
IX	79	185(0.1)	1.5932	0.63	74.55/74.71	7.34/7.39	5.32/5.45	12.28/12.45



III

To reveal a relationship between the structure of the 1,2-aminobutanethiols **IV–IX** we synthesized and their antioxidant activity, we obtained a number of phenyl-substituted 1,2-aminobutanethiols **IV–IX** by reacting 1,2-epithio-4-phenylbutane **III** with various amines:



IV–VI, IX **VII, VIII**

R = C_2H_5, *a* = 0, *b* = 2 (**IV**); R = *n*-C_3H_7, *a* = 1, *b* = 1 (**V**); R = C(CH)$_3$, *a* = 1, *b* = 1 (**VI**); R = C_6H_5, *a* = 1, *b* = 1 (**IX**); X = CH_2 (**VII**); X = O (**VIII**).

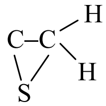
1,2-Aminobutanethiols **IV–VI** were synthesized by reacting **III** with various primary and secondary amines at a 1 : 2 reagent ratio and 70–80°C in the course of 5–6 h in a sealed ampule. All the 1,2-aminobutanethiols **IV–IX** synthesized are colorless fluids turning yellow upon storage. The physicochemical constants of 1-chloro-4-phenyl-2-butanthiol **IV–IX** we obtained are listed in Table 1.

The structure of the compounds synthesized was confirmed by IR and NMR spectroscopies, and their purity was verified by elemental analysis and TLC.

The IR spectrum of the starting thiirane **III** contains no strong bands at 840, 1105, and 1235 cm^{-1}, which characterize asymmetric, symmetric, and pulsation vibrations of the oxirane ring, but there appears a strong absorption band at 625 cm^{-1}, characteristic of stretching vibrations of the C–S bond in the three-membered thiirane ring.

In the IR spectrum of phenyl-substituted 1,2-aminobutanethiols **IV–IX**, we found a very weak band at 2540–2565 cm^{-1}, which corresponds to stretching vibrations of the SH bond and cannot sometimes be detected. In spectra of the compounds synthesized with secondary amino groups we also observed a strong absorption band at 3385 cm^{-1}, which characterizes stretching vibrations of the N–H bond. In addition, all the compounds have absorption bands at around 1065 cm^{-1}, which are related to the C–N bond. The IR spectra of all compounds we synthesized contain absorption bands at 1590–1600 and 1490–1510 cm^{-1}, which can be attributed to stretching vibrations of C=C bonds in the aromatic ring.

The ^{1}H NMR spectrum of thiirane **III**, in which the thiirane ring is separated from the aromatic ring by two methylene groups, signals of the



moiety appear as upfield doublets at 1.85 and 2.25 ppm, which correspond to *cis*- and *trans*-protons. It should be noted that two protons of the methylene groups bonded to the three-membered thiirane ring commonly appear as doublets at 2.10 and 2.45 ppm [4]. The signals of protons of the methylene group bonded to the aromatic ring, which are commonly superimposed by multiplet signals of the CH protons, were found at 2.60–2.75 ppm. In a weak field, protons of aromatic rings appear as a singlet at 6.85–7.00 ppm.

The ^{1}H NMR spectrum of 1-(*N*-diethylamino)-4-phenyl-2-butanethiol (**IV**) contains signals of six protons of two methyl groups in the form of a triplet in its part centered at 1.15 ppm and signals of protons of the $(CH_2)_2NCH_2$ moiety as a multiplet at 2.45 ppm. The signal of the proton of the SH bond was identified on the basis of changes in the spectrum upon addition of D_2O. The nonequivalent protons of the phenylamine moiety appear as two triplets at 6.4 and 6.7 ppm.

The ^{1}H NMR spectra of the rest of the phenyl-substituted 1,2-butanethiols **V–IX** are similar to the spectra of compound **IV**, but, naturally, differ in the positions of radical signals.

The inhibiting properties of phenyl-substituted 1,2-butanethiols **IV–IX** under study were examined in model reactions (Table 2). As the model reaction served the reaction of oxidation in a chlorobenzene solution at 60°C, initiated by α,α-azobisisobutyronitrile (AIBN). The reaction was monitored by the absorption of oxygen in a pressure-gage installation with automatic compensation of the oxygen pressure. The inhibiting properties of the compounds were examined in the reaction with cumyl peroxide radicals and cumyl hydroperoxide.

Our study demonstrated that phenyl-substituted 1,2-butanethiols containing alkylamine (e.g., diethylamine, *n*-propylamine, *tert*-butylamine) or heterocyclic amine-containing moieties (piperidine, morpholine) in their molecule have no effect on the initiated oxidation. However, 1,2-aminobutanethiols **IX** containing a phenylamine moiety hinder the initiated oxidation of cumene.

The reason is that the NH group in the aliphatic chain is not involved in chain-termination reactions and has no effect on the inhibitor efficiency, which depends in this case only on the SH group. It is known that thiols show no antioxidant activity by themselves, with a high antioxidant activity exhibited only when C_6H_5NH and SH groups are combined in the same molecule.

The duration τ of the induction period was used to calculate the stoichiometric coefficient f, equal to the number of oxidation chains terminated at a single molecule of an inhibitor and its conversion products.

The value of the stoichiometric coefficient f for 1-phenyl-4-phenylamino-2-butanethiol **IX** is 2.97. The rate constant of the reaction, $k = 3.12$ l mol^{-1} s^{-1}. It is known that, in the case $f \geq 1$, inhibitors commonly terminate a single oxidation chain. Because the molecule of the inhibitor under study contains amine and sulfhydryl groups, f somewhat exceeds unity.

The reaction of 1-phenyl-4-phenylamino-2-butanethiol **IX** with cumyl hydroperoxide was performed in chlorobenzene in the atmosphere of nitrogen at a temperature of 110°C. It was found that compound **IX** actively decomposes cumyl hydroperoxide. It was shown that one molecule of 1-phenyl-4-phenylamino-2-butanethiol can decompose 15000 molecules of cumyl hydroperoxide.

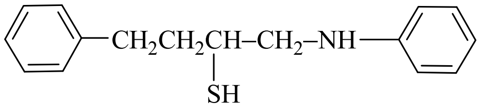
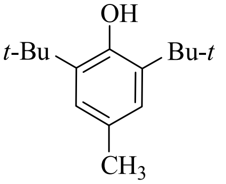
It can be seen in Table 2 that the industrial antioxidant ionol does not decompose cumyl hydroperoxide and is inferior in inhibiting activity to 1-phenyl-4-phenylamino-2-butanethiol because f and k for ionol are 2.00 and 2.10 M^{-1} s^{-1}, respectively.

EXPERIMENTAL

The IR spectra were measured on a Specord 75-IR spectrophotometer, and the ^{1}H NMR spectra, on a Bruker-300 MHz instrument. The individuality and the course of the reactions were monitored by TLC on Silufol UV-254 plates, with a 3 : 1 mixture of heptane and isopropanol used as eluent.

1-Chloro-4-phenyl-2-butanol (I). An ether solution of benzylmagnesium chloride, produced from

Table 2. Kinetic parameters of reaction of compound **IX** with cumyl peroxide (CP) radicals (60°C [AIBN] = 2×10^{-2} M) and with cumyl hydroperoxide (CHP) (110°C) and induction period durations for auto-oxidation of cumene in the presence of this compound (110°C, [InH] = 5×10^{-5} M)

Comp. no.	Formula	CP radicals		CHP		τ, min
		f	$k\times10^{-4}$, M^{-1}	k, M^{-1}	ν	
IX		2.97	3.12	11.8	15000	250
Ionol		2.00	2.10	–		150

63 g (0.5 mol) of benzyl chloride, 12 g of magnesium, 2–3 small iodine crystals, and 30 ml of dry ether, was cooled with ice and a solution of 32.5 g (1 mol) of epichlorohydrin in 200 ml of dry ether was added dropwise under agitation. Then the reaction mixture was heated under permanent agitation at 35°C for additional 2 h. After that, with the flask cooled with ice, a hydrochloric acid solution (10%) was added to the reaction mixture until two transparent layers were formed. The upper organic layer was separated and the aqueous layer was three times extracted with ether. The ether extracts were combined, washed with a dilute soda solution and water, and dried over anhydrous sodium sulfate. After the solvent was evaporated, the reaction product was subjected to vacuum distillation to give 71 g (71%) of compound **I**, bp 161–162°C at 22 mm Hg, n_D^{20} = 1.5354 (published data [5]: bp 158–160°C at 23 mm Hg, n_D^{20} = 1.537).

1,2-Epoxy-4-phenylbutane (II). To a solution of 18.5 g (0.1 mol) of 1-chloro-4-phenyl-2-butanol **I** in 50 ml of dry diethyl ether we added 11.2 g (0.2 mol) of finely ground potassium hydroxide (with a strong warming-up of the reaction mixture observed). Then the mixture was heated on a water bath for 1.5 h. After the mixture was cooled, the ether layer was discharged and the residue was thrice extracted with dry diethyl ether. The ether was evaporated and the reaction product was distilled under a normal pressure to give 11.5 g (75%) of compound **II**, bp 115–116°C at 20 mm Hg (published data [6]: bp 106–109°C at 17 mm Hg).

1,2-Epithio-4-phenylbutane (III). A three-necked flask was charged with 15.2 g (0.2 mol) of thiocarbamide and 6 ml of a sulfuric acid solution (1 equiv of the acid in 350 ml of water). The reaction mixture was cooled under vigorous agitation to 5–10°C and 29.6 g (0.2 mol) of 1,2-epoxy-4-phenylbutane **II** was added dropwise at this temperature in the course of 30 min. Upon addition of oxirane, the reaction mixture was agitated for 1 h at room temperature and neutralized with 21.2 g (0.2 mol) of sodium carbonate dissolved in 10 ml of water. The aqueous layer was separated from the organic layer and extracted with dry ether (2 × 50 ml). The ether extracts were combined with the organic layer and dried over anhydrous sodium sulfate. After the ether was evaporated, vacuum distillation yielded 25 g (76%) of compound **III**, bp 120°C at 2.5 mm Hg, n_D^{20} = 1.5625, R_f = 0.82. Found, %: C 73.31; H 7.12; S 19.16. $C_{10}H_{12}S$. Calculated, %: C 73.12; H 7.35; S 19.52.

IR spectrum, ν, cm^{-1}: 625, 750, 1930. ^1H NMR spectrum, CCl_4, δ, ppm: 2.75 t (2H, ArCH2), 1.85 d and 2.25 d (2H, $6H_2S$), 6.85–7.00 m (5H, C_6H_5).

1-Diethylamino-4-phenyl-2-butanethiol (IV). A mixture of 16.4 g (0.1 mol) of 1,2-epithio-4-phenylbutane **III** and 14.6 g (0.2 mol) of diethylamine was heated in a sealed ampule at 80–90°C for 6 h. Then the ampule was cooled, opened, and the excess amount of diethylamine was distilled off in a vacuum of the water-jet pump. Vacuum distillation yielded 13 g of compound **IV**, bp 110°C at 1 mm Hg, n_D^{20} = 1.5217, R_f = 0.49. Found, %: C 70.51; H 9.89; N 5.73; S 13.85. $C_{14}H_{23}NS$. Calculated, %: C 70.83; H 9.76; N 5.90; S 13.51.

In a similar way, we synthesized aminothiols **V** and **VI**, whose physicochemical constants are listed in Table 1.

4-Phenyl-1-phenylamino-2-butanethiol (IX). To a solution of 9.3 g (0.1 mol) of aniline in 20 ml of benzene, cooled to 10°C, we added 8.2 g (0.05 mol) of 1,2-epithio-4-phenylbutane **III** in the course of 1 h in such a way that the temperature of the reaction mixture did not exceed 10°C. After the addition of thiirane **IV** was complete, the temperature of the reaction mixture was raised first to room temperature and then, on a water bath, to 70–75°C, and the mixture was kept at this temperature for 3 h. Then the solvent was evaporated and the reaction product was subjected to vacuum distillation to give 10 g of compound **IX**, bp 185°C at 1 mm Hg, $n_D^{20} = 1.5932$, $R_f = 0.63$. Found, %: C 70.18; H 7.16; N 5.24; S 11.48. $C_{16}H_{19}NOS$. Calculated, %: C 70.29; H 7.00; N 5.12; S 11.73.

Aminothiols **VII** and **VIII** were synthesized in a similar way.

CONCLUSIONS

(1) A method for synthesis of 1,2-epithio-4-phenylbutane, which is a key compound for production of various phenyl-substituted 1,2-aminobutanethiols, was developed.

(2) It was shown that 1-phenyl-4-phenylamino-2-butanethiol is a complex type inhibitor, which terminates oxidation chains and catalytically decomposes cumyl hydroperoxide.

REFERENCES

1. Kuliev, A.M., *Khimiya i tekhnologiya prisadok k maslam i toplivam* (Chemistry and Technology of Additives to Oils and Fuels), Leningrad: Khimiya, 1985.
2. Rachinskii, F.Yu. and Slachevskaya, N.M., *Khimiya aminotiolov* (Chemistry of Aminothiols), Leningrad: Khimiya, 1965.
3. USSR Inventor's Certificate, no. 118934.
4. Allakhverdiev, M.A., Farzaliev, V.M., and Khalilova, A.Z., *Zh. Org. Khim.,* 1984, vol. 20, no. 6, p. 1350.
5. Malinovskii, M.S., *Okisi olefinov i ikh proizvodnykh* (Oxides of Olefins and Their Derivatives), Moscow: Khimiya, 1961.
6. Levi, J. and Sfiras, Y., *Comp. Rend.*, 1927, vol. 184, p. 1335.