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Correlation between the Structure of Thioureas and Their Reactivity toward Hydroperoxides and Peroxy Radicals

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Abstract—The behavior of thiourea derivatives in reactions simulating oxidative processes in carbon-chain polymers was studied. Based on the kinetic data obtained (reaction rate constants), correlations were revealed between the structures of thioureas and their reactivity in inhibition of oxidation of organic substrates.

Thiourea derivatives are used as thermostabilizers [1, 2] and antioxidants [3] for polymers, in particular, for polyvinyl chloride [4], polyethylene [1], and rubbers [5]. Thiourea derivatives, as a rule, are used as components of mixed stabilizing formulations.

Published data show that thiourea derivatives and formulations are usually chosen empirically, which is apparently due to insufficient understanding of the mechanism of their stabilizing effect and to lack of systematic studies of the structure–inhibiting activity relationship.

Aging of polymers occurs as a branched or degenerately branched chain process [6–8] (Scheme 1), and the reactions responsible for oxidation inhibition can be described by Scheme 2 [9].

Scheme 1.

(a) Initiation of oxidation chains

$$RH + O_2 \longrightarrow R^{\cdot}, \quad (0)$$

(b) Chain propagation

$$R^{\cdot} + O_2 \longrightarrow ROO^{\cdot}, \quad (1)$$

$$ROO^{\cdot} + RH \xrightarrow{k_2} ROOH + R^{\cdot}, \quad (2)$$

(c) Chain branching

$$2ROOH \longrightarrow ROO^{\cdot} + H_2O + RO^{\cdot}, \quad (3)$$

$$ROOH + RH \longrightarrow ROO^{\cdot} + H_2O + R^{\cdot}, \quad (4)$$

$$ROOH \longrightarrow RO^{\cdot} + HO^{\cdot}, \quad (5)$$

(d) Chain termination

$$2ROO^{\cdot} \longrightarrow \text{Reaction products}. \quad (6)$$

Scheme 2.

$$ROO^{\cdot} + InH \xrightarrow{k_7} ROOH + In^{\cdot}, \quad (7)$$

$$InH + ROOH \longrightarrow \text{Molecular products}, \quad (8)$$

$$InH + ROOH \longrightarrow \text{Free radicals}. \quad (9)$$

Therefore, it seemed appropriate to study the behavior of thiourea derivatives in reactions with species similar to primary products of hydrocarbon oxidation: peroxy radicals and hydroperoxides [9].

As an example, we studied the reactions of thiourea derivatives with cumene hydroperoxide. In this case, the stabilizing effect is characterized by the rate constant k of the reaction of the inhibitor with the hydroperoxide [10] and by the stoichiometric coefficient ν denoting the number of hydroperoxide molecules decomposed by one inhibitor molecule.

Our studies showed that cumene hydroperoxide (CHP) starts to react with arylthioureas **I**–**IX** at a noticeable rate above 50°C, as judged from variation of the ^{1}H NMR chemical shifts. For example, in the spectrum of the reaction mixture (CHP : **I** ratio 2 : 1) in deuteromethanol at room temperature, no changes were observed in 5 h, and at 50°C the reaction occurred to only 20–25% in 5 h, as indicated by a decrease in the intensity of the signals of methyl protons in cumene hydroperoxide in the range 1.75–1.92 ppm. In DMSO-d_6, this reaction at 50°C and the same reactant ratio did not occur at all.

Thiourea derivatives **X**–**XIV** containing the benzoyl fragment readily react with cumene hydroperoxide even at room temperature.

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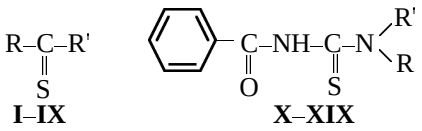
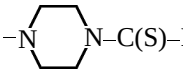
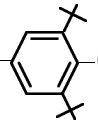
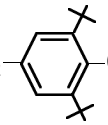
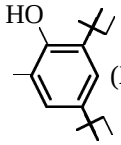
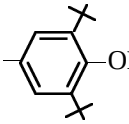
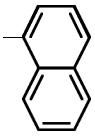


I–IX **X–XIX**

R = R' = H_2N (**I**), HNPh (**II**); R = HNPh, R' = NHC_6H_4-*p*-CH_3 (**III**),  (**IV**),  (**V**),

$NHCH_2CH_2NHC(S)NHPh$ (**VI**); R = $NHCH_2$  , R' = HNPh (**VII**), NH_2 (**IX**); R = $NH(CH_2)_2$  ,

R' = NH_2 (**VIII**); R = H, R' =  (**X**), CH_2  (**XI**),  (**XII**); NRR' =  (**XIII**),

 (**XIV**).

Table 1. Stoichiometric coefficients ν and rate constants k ($l\ mol^{-1}\ s^{-1}$) of reactions of thioureas with cumene hydroperoxide (CHP) (80°C, 2-PrOH)

Comp. no.	ν_{CHP}	$k \times 10$	Comp. no.	ν_{CHP}	$k \times 10$
I	10	0.41	**VI**	180	0.58
II	40	0.45	**VII**	250	0.75
III	40	0.42	**VIII**	250	0.73
IV	50	0.47	**IX**	500	0.87
V	140	0.55			

The corresponding kinetic parameters are given in Tables 1 and 2.

The curves of cumene hydroperoxide consumption with time (Figs. 1, 2) showed induction periods neither for arylthioureas **I**–**IX**, nor for benzoylthioureas **X**–**XIV**. This fact indicates that the starting compounds are primary reactive species with respect to the hydroperoxide.

Apparently, the process is catalytic, as suggested by very large values of ν for the reactions of thiourea derivatives with cumene hydroperoxide (Tables 1, 2).

It is known that hydroperoxides under the action of inhibitors can decompose by both homolytic and heterolytic mechanisms [11, 12]. For inhibiting the oxidation, the heterolytic mechanism is preferable [12].

To reveal the nature of the reactions of cumene hydroperoxide with thiourea derivatives, we added to the reaction mixture a radical acceptor, 2,6-di-*tert*-butyl-4-methylphenol (Ionol), in view of the fact that phenolic stabilizers, and Ionol in particular, inhibit oxidation of hydrocarbons owing to reaction (10) with peroxy radicals [13]:

Table 2. Kinetic and stoichiometric parameters of reactions of cumene hydroperoxide (CHP)[a] with benzoylthioureas; steric (R_S) and inductive ($\Sigma\sigma^*$) constants of substituents at the reaction center (N^3)

Comp. no.	ν,[b] 100°C	E_a, kJ mol^{-1}	log A_0	k, $mol^{-1.5}\ l^{1.5}\ s^{-1}$			R_S	$\Sigma\sigma^*$
				30°C	50°C	100°C		
X	12 000	22.84	3.53	0.27	0.93	1.87	–6.67	1.12
XI	8000	16.10	2.51	0.48	0.80	1.66	–6.03	–1.57
XII	13 000	22.94	3.63	0.33	0.68	1.66	–6.21	0.31
XIII	9000	18.05	2.75	0.44	0.68	1.35	–6.63	–2.96
XIV	5000	19.94	3.84	0.24	0.42	1.12	–7.59	–3.51

[a] [CHP] 1×10^{-1} M, clorobenzene, 30–100°C. [b] (ν) Stoichiometric coefficient of the reactions of benzoylthioureas with cumene hydroperoxide.

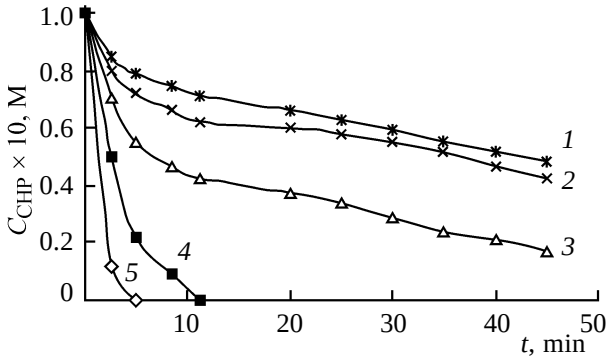


Fig. 1. Kinetic curves of cumene hydroperoxide (CHP) consumption under the action of arylthioureas (ATUs) ([ATU] 1×10^{-1} M, 80°C, 2-propanol): (*1*) **II** and **III**, (*2*) **IV**, (*3*) **V**, (*4*) **VII** and **IX**, and (*5*) **VIII**.

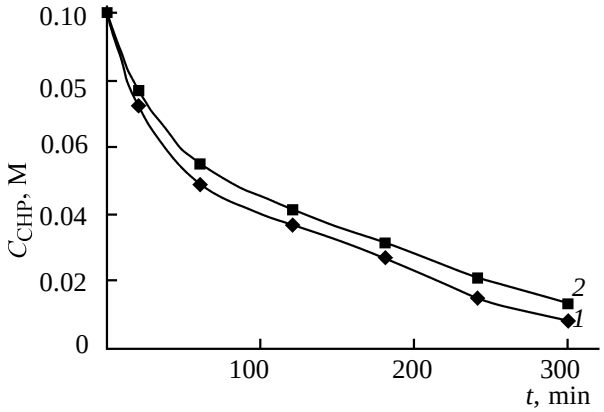


Fig. 2. Kinetic curves of cumene hydroperoxide (CHP) consumption under the action of arylthiourea **IX** ([**IX**] 5×10^{-3} M, [Ionol] 5×10^{-2} M, 80°C, 2-propanol): (*1*) **IX** and (*2*) **IX** + Ionol.

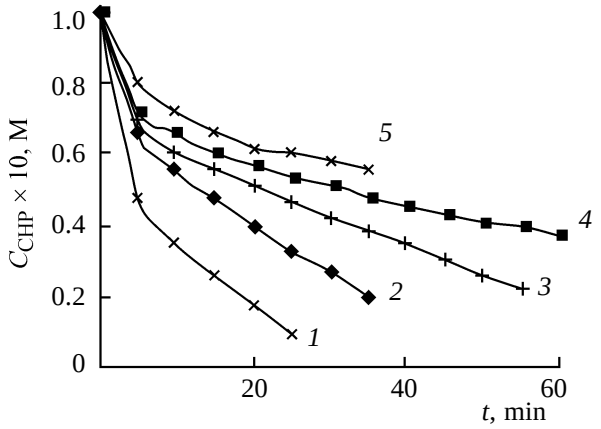


Fig. 3. Kinetic curves of cumene hydroperoxide (CHP) consumption under the action of benzoylthioureas (BTUs) ([BTU] 1×10^{-2} M, 100°C, chlorobenzene): (*1*) **X**, (*2*) **XII**, (*3*) **XI**, (*4*) **XIV**, and (*5*) **XIII**.

$$PhOH + RO_2^{\cdot} \longrightarrow PhO^{\cdot} + ROOH. \quad (10)$$

In the case of the homolytic pathway, the rate of hydroperoxide consumption in the presence of the inhibitor will decrease when the system contains radical species [10].

Addition of Ionol to the reaction mixture did not noticeably affect the rate of cumene hydroperoxide decomposition (Fig. 3), which suggest that the heterolytic mechanism of the process prevailed.

The partial orders of the reactions of aryl- and benzoylthioureas with cumene hydroperoxide, determined by the differential method from the dependence of the initial reaction rate on the initial reactant concentrations [14] [Eqs. (11), (12)], show that the reaction in both cases is first-order with respect to cumene hydroperoxide, but the orders with respect to thiourea derivatives are different: with arylthioureas (ATUs), the reaction is first-order, and with benzoylthioureas (BTUs), the order is fractional, suggesting a complex reaction mechanism.

The initial reaction rate was described by Eqs. (11) and (12):

$$\omega_0 = k[CHP][ATU], \quad (11)$$

$$\omega_0 = k[CHP][BTU]^{1.5}. \quad (12)$$

The kinetic and stoichiometric parameters obtained (Tables 1, 2) show that the rate constants of the reactions of benzoylthioureas with cumene hydroperoxide and the stoichiometric coefficients are higher than the respective parameters for arylthioureas, suggesting higher activity of benzoylthioureas in decomposition of the hydroperoxide.

Using the rate constants *k* obtained, we constructed the structure–reactivity correlation. To this end, we used the semiempirical model of the frontal steric effect, which allows adequate and accurate calculation of the steric effect of any substituent at any reaction center [15–18].

The model is based on the principle of mechanical shielding of a reaction center with substituents preventing access of the second reactant.

The solutions (correlation equations) were sought for in the form of two-parameter correlation equations

$$\log k = a_0 + a_1\Sigma\sigma^* + a_3R_S, \quad (13)$$

where *k* is the rate constant of the reaction of thiourea derivatives with cumene hydroperoxide, R_S are the steric constants, and σ^* are the Taft inductive con-

stants of substituents at the noncarbon reaction center, calculated theoretically [14] as

$$\sigma^* = 7.840\Sigma\Delta\chi R_i^2/r_i^2. \quad (14)$$

Here, R_i is the covalent radius of *i*th atom, r_i is its distance from the reaction center, and $\Delta\chi_i$ is the difference between the electronegativities of the *i*th atom and reaction center.

All the theoretical parameters used in this study (σ^*, R_S, group electronegativities) were calculated from basic physical and geometric parameters (bond angles, bond lengths, atom electronegativities).

The rate constants k of the reactions of thiourea derivatives with the hydroperoxide, Taft inductive constants σ^*, and steric constants R_S are listed in Table 2. For the examined benzoylthioureas, there is a good correlation ($r \geq 0.98$) of $\log k$ with the calculated constants of substituents at the N^3 atom [Eqs. (15)–(17)]:

$$\log k(30) = (-0.048 \pm 0.012)\Sigma\sigma^* + (0.244 \pm 0.040)R_S + (1.087 \pm 0.257);\ r\ 0.9749,\ S_0\ 0.041,\ N\ 5, \quad (15)$$

$$\log k(50) = (0.010 \pm 0.006)\Sigma\sigma^* + (0.160 \pm 0.019)R_S + (-1.213 \pm 0.121);\ r\ 0.9808,\ S_0\ 0.023,\ N\ 5, \quad (16)$$

$$\log k(100) = (0.031 \pm 0.008)\Sigma\sigma^* + (0.056 \pm 0.028)R_S + (0.593 \pm 0.179);\ r\ 0.9732,\ S_0\ 0.028,\ N\ 5. \quad (17)$$

Here, the figures in parentheses at k denote the temperature, °C.

The rate of cumene hydroperoxide consumption under the action of benzoylthiourea derivatives depends on the electronic and, to a greater extent, steric effects of substituents, as indicated by the coefficients at σ^* and R_S. The rate constants of the reactions of benzoylthioureas with the hydroperoxide decrease as the steric eeffect of substituents at N^3 becomes stronger. With increasing temperature, the effect of the steric factor becomes less significant, which follows from a decrease in the coefficient at R_S in Eqs. (15)–(17), whereas the significance (contribution) of the electronic effect increases (the coefficient at $\Sigma\sigma^*$ grows).

Within the framework of the suggested steric model, we established a correlation between the structure of thiourea derivatives and their inhibiting activity in reactions with peroxy radicals. Kinetic experiments were performed under conditions of the model reaction of liquid-phase oxidation of styrene. The efficiency of oxidation inhibition is characterized in this case [10] by the rate constants of the reaction of the inhibitor with $RO_2^{\cdot}$ radicals (k_7, Table 3).

Table 3. Logarithms of rate constants[a] and steric (R_S) and inductive ($\Sigma\sigma^*$) constants of substituents at the reaction center (N) of arylthioureas

Comp. no.	log k_7	R_S	$\Sigma\sigma^*$
III	4.78	–5.00	0.50
IV	4.73	–4.53	–3.34
VII	5.48	–4.45	0.15
VIII	6.00	–3.55	–0.94
IX	6.48	–3.23	–1.00

[a] Styrene, 50°C, initiator azobis(isobutyronitrile), 2.5×10^{-3} M; k_7 is the rate constant of the reaction of arylthiourea with peroxy radicals.

The relationship between k_7 of arylthioureas and the steric (R_S) and electronic (σ^*) effects of varied substituents at the nitrogen atom is described by a two-parameter equation (18) with an excellent correlation coefficient (r 0.99):

$$\log k_7 = (0.160 \pm 0.044)\Sigma\sigma^* + (1.028 \pm 0.090)R_S + (9.909 \pm 0.387);\ r\ 0.9926,\ S_0\ 0.131,\ N\ 5. \quad (18)$$

This fact suggests that the most probable reaction center in this process is the nitrogen atom.

Correlation (18) shows that the rate constant of the reaction of arylthioureas with peroxy radicals decreases with increasing steric effect of substituents at the nitrogen atom (Table 3).

Thus, our results show that there is a statistically significant correlation between the structure of thiourea derivatives and their reactivity toward peroxy radicals and hydroperoxides. These results can serve as a basis for designing effective oxidation inhibitors.

EXPERIMENTAL

The kinetics of the reactions of thiourea derivatives with cumene hydroperoxides (reaction orders, rate constants, etc.) were monitored by iodometric titration (2-propanol) [19], kinetic polarography (chlorobenzene) [20], and ^{1}H NMR spectroscopy (DMSO-d_6 or CD_3OD; Gemini-200 spectrometer, working frequency 200 MHz) in the range 20–100°C. The reactions were performed in CD_3OD or DMSO-d_6 at 20–50°C; the ratio of cumene hydroperoxide to arylthiourea was 20 : 1.

The stoichiometry of hydroperoxide consumption ν was determined by iodometric titration and polarography in the following concentration ranges: cumene

hydroperoxide 1.0–0.5 M and thiourea derivatives 1×10^{-1}–1×10^{-5} M. The accuracy of the polarographic analysis was 5%.

The stoichiometric coefficient ν was calculated as follows:

$$\nu = \frac{[ROOH]_0 - [ROOH]_\infty}{[InH]_0}, \qquad (19)$$

where $[ROOH]_0$ and $[ROOH]_\infty$ are the initial and final concentrations of cumene hydroperoxide, respectively, and $[InH]_0$ is the initial concentration of arylthiourea.

The contribution of the radical reaction pathway was estimated according to [12].

The reaction orders with respect to each reactant were determined according to [14].

Initiated oxidation of styrene [10] was performed at the initial oxygen pressure of 250 mm at 50°C. The sensitivity of the installation to variation of the oxygen pressure was 2×10^{-4} M per 1 mm of the oxygen taken up. As initiator in styrene oxidation we used azobis(isobutyronitrile) (2.5×10^{-3} M). The inhibitor concentration was varied within 1×10^{-2}–2.5×10^{-3} M. Under the experimental conditions, the oxidation was kinetically controlled. The mean error of determining k_7 was 7%.

All the theoretical parameters used in this study (σ*, R_S, group electronegativities) were calculated from the basic physical and geometric parameters (bond angles, bond lengths, atom electronegativities) using Hyper Chem 5.0 software. If necessary, the molecular geometry was estimated by molecular-mechanical and semiempirical quantum-chemical calculations using the methods included in Hyper Chem 5.0 (MM+, AM1, PM3). All the statistical and graphic calculations were performed using standard software (Statgraphics, Statistica, Excel).

The intramolecular distances were determined in the approximation of the least eclipsed conformations of the compounds using standard values of bond angles and lengths. The correlation analysis was performed by the least-squares method.

REFERENCES

1. Voigt, J., *Die Stabilisierung der Kunststoffe gegen Licht und Wärme*, Berlin: Springer, 1966.
2. US Patent 3547879, 1972, *Ref. Zh. Khim.*, 1973, 9S502.
3. Mukmeneva, N.A., Cherezova, E.N., and Tuzova, N.G., *Zh. Prikl. Khim.*, 1994, vol. 67, no. 4, p. 633.
4. Minsker, K.S. and Fedoseeva, G.T., *Destruktsiya i stabilizatsiya polivinilkhlorida* (Degradation and Stabilization of Polyvinyl Chloride), Moscow: Khimiya, 1979.
5. Angert, L.G., *Kauchuk Rezina*, 1980, no. 4, p. 46.
6. Emanuel', N.M., *Usp. Khim.*, 1979, vol. 48, no. 12, p. 2113.
7. Denisov, E.T., *Usp. Khim.*, 1978, vol. 47, no. 6, p. 1090.
8. Emanuel', N.M., Denisov, E.T., and Maizus, Z.K., *Tsepnye reaktsii okisleniya uglevodorodov v zhidkoi faze* (Chain Reactions of Liquid-Phase Oxidation of Hydrocarbons), Moscow: Nauka, 1965.
9. Emanuel', N.M. and Buchachenko, A.L., *Khimicheskaya fizika stareniya i stabilizatsii polimerov* (Chemical Physics of Aging and Stabilization of Polymers), Moscow: Nauka, 1982.
10. Denisov, E.T. and Azatyan, V.V., *Ingibirovanie tsepnykh reaktsii* (Inhibition of Chain Reactions), Chernogolovka, 1997.
11. Leonov, V.N., Stozhkova, G.A., and Bobylev, B.N., *Neftekhimiya*, 1987, vol. 27, no. 5, p. 710.
12. Sanin, P.I., Sher, V.V., and Shkhiyants, I.V., *Neftekhimiya*, 1978, vol. 18, no. 5, p. 693.
13. Roginskii, V.A., *Fenol'nye antioksidanty* (Phenolic Antioxidants), Moscow: Nauka, 1988.
14. Denisov, E.T., *Kinetika gomogennykh khimicheskikh reaktsii* (Kinetics of Homogeneous Chemical Reactions), Moscow: Vysshaya Shkola, 1978.
15. Galkin, V.I., Sayakhov, R.D., and Cherkasov, R.A., *Usp. Khim.*, 1991, vol. 60, no. 8, p. 1617.
16. Galkin, V.I. and Cherkasov, R.A., *Reakts. Sposobn. Org. Soedin.*, 1981, vol. 18, no. 1, p. 111.
17. Zyablikova, T.A. and Buzykin, B.I., *Zh. Obshch. Khim.*, 1996, vol. 66, no. 3, p. 470.
18. Vereshchagin, A.N., *Induktivnyi effekt* (Inductive Effect), Moscow: Nauka, 1987.
19. Antonovskii, V.M. and Buzlakova, M.M., *Analiticheskaya khimiya organicheskikh peroksidnykh soedinenii* (Analytical Chemistry of Organic Peroxy Compounds), Moscow: Khimiya, 1978.
20. Chebotareva, E.G., Pobedimskii, D.G., and Kolyubakina, N.S., *Kinet. Katal.*, 1983, vol. 14, no. 4, p. 981.