ISSN 1070-4272, Russian Journal of Applied Chemistry, 2011, Vol. 84, No. 8, pp. 1394–1397. © Pleiades Publishing, Ltd., 2011. Original Russian Text © A.R. Sudzhaev, I.A. Rzaeva, R.A. Nadzhafova, Yu.S. Safarov, M.A. Allakhverdiev, 2011, published in Zhurnal Prikladnoi Khimii, 2011, Vol. 84, No. 8, pp. 1329–1332.

> \_\_\_\_\_ ORGANIC SYNTHESIS AND INDUSTRIAL \_\_ ORGANIC CHEMISTRY

# **Antioxidant Properties of Some Thiourea Derivatives**

A. R. Sudzhaev, I. A. Rzaeva, R. A. Nadzhafova, Yu. S. Safarov, and M. A. Allakhverdiev

Kuliev Institute of Chemistry of Additives, National Academy of Sciences of Azerbaijan, Baku, Azerbaijan

Received October 22, 2010

Abstract—Antioxidant properties of some thiourea derivatives in model reactions were studied.

**DOI:** 10.1134/S1070427211080167

Proceeding with studies in the field of synthesis [1, 2] and antioxidant properties [3–5] of thiourea derivatives, we synthesized some thiourea derivatives and examined their antioxidant properties in model reactions.

Our experiments showed that the reaction of thiourea with ethanolamine yields 1-(2-aminoethyl) thiourea I.

Similarly, the reaction of thiourea with diethanol-

amine yields N,N-(iminodiethane-2,1-diyl)bis(thiourea) II.

An increase in the amount of thiourea taken for the reaction leads to the substitution of both hydroxy groups in the diethanolamine molecule by thiourea residues.

The reaction of 1-(*N*-phenylamino)-2-propanol with thiourea yields 1-[1-methyl-2-(phenylamino)ethyl)] thiourea **III**.



The reaction is usually accompanied by the heat release, with the temperature of the reaction mixture reaching 80–90°C. At this temperature, after heating for 1 h, 1-[1-methyl-2-(phenylamino)ethyl)]thiourea **III** is formed in 82% yield. This compound is liquid

and can be distilled in a vacuum. After a certain time, it crystallizes to form fine crystals.

To evaluate the antioxidant activity of thiourea derivatives I–III, we used a comprehensively studied



**Fig. 1.** Kinetic curves of cumene autooxidation with the participation of **I–III**.  $T = 110^{\circ}$ C,  $[InH] = 5 \times 10^{-5}$  M.  $[V(O_2)]$  Volume of oxygen taken up and (*t*) time; the same for Fig. 2. (*I'*) No inhibitor; (*I–3*) oxidation in the presence of **I–III**, respectively; the same for Fig. 2.

reaction of cumene oxidation. A study of the cumene autooxidation in the presence of these compounds showed that they inhibit the autooxidation. Figure 1 shows the kinetic curves of cumene oxidation in the presence of I–III at 110°C.

We studied the reactions of **I–III** with cumylperoxy radicals at a constant initiator (AIBN) concentration of  $2 \times 10^{-2}$  M and temperature of 60°C. The kinetic curves of the initiated cumene oxidation in the presence of **I–III** show that these compounds terminate the oxidation chain in the reaction with cumylperoxy radicals (Fig. 2).

From the length of the induction period  $\tau$  (min), we calculated the stoichiometric inhibition coefficient *f*. This parameter is equal to the number of oxidation chains terminated on one inhibitor molecule and its transformation products and is calculated by the formula

#### $f = (\tau W_{\rm i})/[{\rm InH}]_0,$

where  $W_i$  is the initiation rate,  $2 \times 10^{-7}$  mol l<sup>-1</sup> s<sup>-1</sup>; [InH]<sub>0</sub>, initial inhibitor concentration,  $5 \times 10^{-4}$  M.

From the kinetics of the oxygen uptake, we calculated the rate constant of the reaction of the inhibitor with cumylperoxy radicals  $k_7$ . To determine  $k_7$ , the kinetic curves of the initiated cumene oxidation were transformed from the coordinates  $\Delta[O_2]^{-1} - t^{-1}$ , and from the slope of the straight line [7].



**Fig. 2.** Kinetic curves of initiated oxidation of cumene in the presence of **I–III**.  $T = 60^{\circ}$ C, [InH] =  $5 \times 10^{-4}$  M.

$$\tan \alpha = \frac{fk_7[\text{InH}]_0}{k_2[\text{RH}]W_i}$$

we found

$$k_7 = \frac{\tan \alpha k_2 [\text{RH}] W_i}{f [\text{InH}]_0}$$

where  $k_2$  is the rate constant of the reaction of the RO<sub>2</sub> radical with the hydrocarbon molecule at 60°C, 1.5 l mol<sup>-1</sup> s<sup>-1</sup>; [RH] = 7.17 M for neat cumene [8].

The kinetic parameters characterizing the antioxidant properties of **I–III** are given in the table.

As seen from the table, the stoichiometric inhibition coefficients f of **I–III** vary within 3.6–5.04, with the highest value observed with N,N'-(iminodiethane-2,1-diyl)bis(thiourea) **II**.

The induction period with this compound is relatively long, 265 min. The inhibition rate constant  $k_7$  for **II** is  $3.26 \times 10^4 \text{ l mol}^{-1} \text{ s}^{-1}$ . Similarly, for **I**,  $k_7$  is  $2.28 \times 10^4$ , and for **III**,  $2.56 \times 10^4 \text{ l mol}^{-1} \text{ s}^{-1}$ .

The reactions of **I–III** with cumyl hydroperoxide (CHP) were performed at 110°C in chlorobenzene solution in a nitrogen atmosphere. We found that compounds **I–III** catalytically decompose cumyl hydroperoxide. The kinetic curve of the decomposition of  $N,N^{-}$ (iminodiethane-2,1-diyl)bis(thiourea) **II** is shown in Fig. 3.

The catalytic factor v given in the table shows how many CHP molecules decompose under the action of



**Fig. 3.** Kinetic curve of cumyl hydroperoxide decomposition in the presence of *N*,*N*-(iminodiethane-2,1-diyl)bis-(thiourea) II.  $T = 110^{\circ}$ C, [InH] =  $5 \times 10^{-4}$  M. ([ROOH], M) Cumyl hydroperoxide concentration and (*t*) time.

one inhibitor molecule and its transformation products. This is clear from the following formula:

$$\nu = \frac{[\text{ROOH}]_0 - [\text{ROOH}]_{\infty}}{[\text{InH}]_0} ,$$

where  $[ROOH]_0$  is the initial, and  $[ROOH]_{\infty}$ , final CHP concentration.

Summarizing the results obtained, we can note that the antioxidant properties of substituted thioureas are gradually enhanced with an increase in the number of nitrogen atoms in the molecule. Analysis of the kinetic parameters of the cumyl hydroperoxide decomposition shows that the catalytic activity depends on the structure of the compounds. The highest catalytic factor,  $v = 22\,000$ , is observed for **II**. Compound **III** also shows relatively high activity:  $v = 20\,000$ . 1-(2-Aminoethyl)thiourea is the least active:  $v = 17\,000$ . The rate constant *k* of cumyl hydroperoxide decomposition depends on the antioxidant structure. Antioxidants **I–III** are characterized not only by high catalytic factors, but also by high rate constants. For example, at 110°C, *k* for **II** is 11, and for **I**, 10.5 1 mol<sup>-1</sup> s<sup>-1</sup>.

Thus, thiourea derivatives **I–III**, showing increased activity as inhibitors, not only catalytically decompose cumyl hydroperoxide, but also react with cumylperoxy radicals, terminating oxidation chains.

#### **EXPERIMENTAL**

The structures of the compounds synthesized were determined by IR and <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy and by liquid chromatography. The purity of the compounds was checked by thin-layer chromatography on Silufol UV-254 plates. As eluent we used a mixture of isopropyl alcohol with hexane (3 : 5). In each case, one spot was observed after exposure to iodine vapor.

**1-(2-Aminoethyl)thiourea I.** A flask was charged with a mixture of 6.1 g (0.1 mol) of ethanolamine, 7.6 g (0.1 mol) of thiourea, and 10 ml of trifluoroacetic acid. The mixture was stirred for 11 h at  $45-50^{\circ}$ C. The reaction progress was monitored by thin-layer

Comp. no.	Formula	$T = 60^{\circ}\mathrm{C}$		$T = 110^{\circ} \text{C}$		
		f	$k_7 \times 10^{-4}, \\ 1 \text{ mol}^{-1} \text{ s}^{-1}$	$k, \\ 1 \text{ mol}^{-1} \text{ s}^{-1}$	ν	τ, min
Ι	NH <sub>2</sub>	3.6	2.28	8.6	17000	200
	HN NH <sub>2</sub> S					
II	NH	5.04	3.26	11	22000	265
	$\begin{array}{c c} HN & HN & HN & HN \\ S & S & S \\ \end{array}$					
III		3.84	2.56	10.5	20000	220
	NH					
	HN NH <sub>2</sub>					
	II S					

Kinetic parameters of reactions of I-III with cumylperoxy radicals and of cumyl hydroperoxide decomposition

chromatography. After the reaction completion, trifluoroacetic acid was distilled off. The organic product was extracted with  $CCl_4$  and ether. 1-(2-Aminoethyl)thiourea I was obtained in 58% yield, mp 108°C,  $R_f$  0.21. Found, %: C 30.18, H 7.72, N 35.19, S 26.85. C<sub>3</sub>H<sub>9</sub>N<sub>3</sub>S. Calculated, %: C 30.23, H 7.61, N 35.26, S 26.90.

*N,N*'-(Iminodiethane-2,1-diyl)bis(thiourea) II was prepared similarly. A flask was charged with a mixture of 4.2 g (0.04 mol) of diethanolamine, 3.04 g (0.04 mol) of thiourea, and 5 ml of trifluoroacetic acid. The mixture was stirred for 8 h at 40–45°C. The reaction progress was monitored by thin-layer chromatography. After the reaction completion, trifluoroacetic acid was distilled off. The product, *N,N*-(iminodiethane-2,1-diyl)bis(thiourea) II, was crystallized from ethanol. Yield 90%, mp 119°C,  $R_f$  0.34. Found, %: C 32.49, H 6.94, N 31.59, S 28.88.C<sub>6</sub>H<sub>15</sub>N<sub>5</sub>S<sub>2</sub>. Calculated, %: C 32.56, H 6.83, N 31.64, S 28.97.

Compound **III** was prepared similarly from 7.6 g (0.1 mol) of thiourea and 15.1 g (0.1 mol) of 1-(*N*-phenylamino)-2-propanol. Yield 10 g (82%), mp 145°C,  $R_{\rm f}$  0.53. Found, %: C 57.38, H 7.23, N 20.01, S 15.27. C<sub>10</sub>H<sub>15</sub>N<sub>3</sub>S. Calculated, %: C 57.42, H 7.18, N 20.09, S 15.31.

## CONCLUSIONS

(1) A series of thiourea derivatives were synthesized. (2) These compounds take active part in scavenging of cumylperoxy radicals and simultaneously effect catalytic decomposition of cumyl hydroperoxide.

### REFERENCES

- Magerramov, A.M., Mekhtieva, G.R., Abdinbekova, R.T., et al., *Vestn. Bakinsk. Univ., Ser. Estestv. Nauk*, 2002, no. 3, pp. 5–10.
- 2. Magerramov, A.M., Abdinbekova, R.T., Kurbanova, M.M., et al., *Processes Petrochem. Refin.*, 2003, no. 3, p. 50.
- Farzaliev, V.M., Allakhverdiev, M.A., and Rzaeva, I.A., *Zh. Prikl. Khim.*, 1994, vol. 67, no. 6, pp. 1025–1028.
- Farzaliev, V.M., Allakhverdiev, M.A., and Rzaev, I.A., Neftekhimiya, 1998, vol. 38, no. 2, p. 137.
- Farzaliev, V.M., Magerramov, A.M., Allakhverdiev, M.A., and Rzaev, I.A., *Zh. Prikl. Khim.*, 2001, vol. 74, no. 1, pp. 110–113.
- Sudzhaev, A.R., Nadzhafova, R.A., Allakhverdiev, M.A., and Safarov, Yu.S., *Nauchn. Novosti*, 2007, no. 2, pp. 36–40.
- Denisov, E.T., Kharitonov, V.V., and Fedorov, V.V., Metod transformatsii kineticheskikh krivykh kak sposob otsenki effektivnosti ingibitorov okisleniya (Transformation of Kinetic Curves as a Method for Evaluating the Performance of Oxidation Inhibitors), Chernogolovka, 1973.
- 8. Denisov, E.T., *Konstanty skorosti gomoliticheskikh zhidkofaznykh reaktsii* (Rate Constants of Homolytic Liquid-Phase Reactions), Moscow: Nauka, 1971.