ISSN 1070-4272, Russian Journal of Applied Chemistry, 2012, Vol. 85, No. 4, pp. 644–650. © Pleiades Publishing, Ltd., 2012. Original Russian Text © A.M. Magerramov, A.R. Askerova, E.Ya. Mamedov, I.A. Rzaeva, M.A. Allakhverdiev, 2012, published in Zhurnal Prikladnoi Khimii, 2012, Vol. 85, No. 4, pp. 628–634.

> ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

3,5-Di-*tert*-butyl-4-hydroxybenzaldehyde Derivatives as Antioxidants in Cumene Oxidation

A. M. Magerramov, A. R. Askerova, E. Ya. Mamedov, I. A. Rzaeva, and M. A. Allakhverdiev

> Baku State University, Baku, Azerbaijan e-mail: rector@bsu.edu.az

> > Received August 17, 2010

Abstract—A series of 4-hydroxy-3,5-di-*tert*-butylbenzaldehyde derivatives were prepared, and their antioxidant properties were studied.

DOI: 10.1134/S1070427212040180

Sterically hindered phenols are strong antioxidants and efficiently inhibit oxidation of various organic compounds. They readily react with peroxy radicals and terminate oxidation chains [1]. Proceeding with studies in the field of synthesis and antioxidant behavior of sulfur-containing additives [2–6], we prepared in this

work a series of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (1) derivatives.

Condensation of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde **1** with hydantoin gives hydantoin-substituted 2,6-di-*tert*-butylphenol **2**:





where $+ = (CH_3)_3C$.

The reaction of 4-arylthiazolamine with 3,5-di-tert-







Ternary condensation of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde, thiourea, and various amines yields 2,6-bis(3,5-di-*tert*-butyl-4-hydroxyphenyl)hexahydro-1,3,5-triazine-4-thiones **4** and 5 (Scheme 1). Methylene-active carbonyl and dicarbonyl compounds such as ethyl cyanoacetate, hydantoin, acetylacetone, and dimedone enter into ternary condensation with 3,5-di-*tert*butyl-4-hydroxybenzaldehyde and 4-aryl-2-thiazolamine

Scheme 1.



H (4), HOCH₂CH₂ (5).





to form the corresponding derivatives. The ternary condensation usually follows Scheme 2.

All the synthesized compounds are yellow crystals or oily masses soluble in many organic solvents. They were usually recrystallized from alcohols. The physicochemical constants and analytical data are given in Table 1.

The structures of the compounds synthesized were proved by IR and ¹H and ¹³C NMR spectroscopy. The purity was checked by elemental analysis and TLC.

The IR spectra of the compounds do not contain an absorption band at 3615 cm⁻¹, noted in [1]. In the IR spectra of all the compounds, the phenolic hydroxyl band was observed at 3190–3220 cm⁻¹. The absorption bands at 1690, 1750, and 1790 cm⁻¹ are characteristic of the CO bond in cyclic amides. In the IR spectrum of 2, the absorption bands at 1430 and 1450 cm⁻¹ correspond to vibrations of the C–N bonds, and those at 690–810 and 820 cm⁻¹, to out-of-plane wagging vibrations of the NH bond.

In the IR spectrum of azomethine **3**, the absorption bands at 1620 and 1660 cm⁻¹ correspond to C=N, and that at 1040 cm⁻¹, to C–N stretching vibrations.

In the IR spectra of 2,6-bis(3,5-di-*tert*-butyl-4hydroxyphenyl)hexahydro-1,3,5-triazine-4-thiones 4 and 5, the C=S stretching vibrations are manifested at 1225–1190 cm⁻¹. In contrast to the C=O band, the C=S band in some cases is difficult to reveal. The NHCSNH bands are manifested at 1335–1265 cm⁻¹ [7]. In the IR spectra of ternary condensation products **6** and **7** with acetylacetone, the absorption band at 1575–1620 cm⁻¹ corresponds to stretching vibrations of the enol carbonyl group C=O. The other IR spectra are similar to those of **2**.

In the ¹H NMR spectrum of the initial 3,5-di-*tert*butyl-4-hydroxybenzaldehyde **1**, 18 H atoms give a singlet at 1.5–1.8 ppm. Two protons of the aromatic ring give a singlet at approximately 8 ppm. We also revealed the signal from the aldehyde proton (1 H) at 10.25 ppm.

Compound	Yield, %	<i>T</i> , °C	Found, %/Calculated, %				En ministra 1 Communitor	D
			С	Н	N	S	Empirical formula	ĸ _f
2	86	150–151	<u>64.62</u> 64.84	<u>6.76</u> 6.95	$\frac{4.47}{4.20}$	<u>9.48</u> 9.62	C ₁₈ H ₁₃ NO ₃ S	0.61
3	83	103–104	<u>72.63</u> 72.32	<u>8.35</u> 8.60	<u>7.28</u> 7.03	<u>8.01</u> 8.04	$C_{25}H_{28}N_2OS$	0.45
4	35	147–148	<u>70.98</u> 70.81	<u>8.85</u> 9.01	<u>7.72</u> 7.99	<u>6.28</u> 6.10	$C_{31}H_{47}N_3O_2S$	0.45
5	46	127–128	<u>74.81</u> 74.29	<u>10.54</u> 10.31	<u>5.66</u> 5.30	$\frac{4.43}{4.05}$	$C_{33}H_{47}N_3O_3S$	0.87
6	22	132–133	<u>65.27</u> 65.46	<u>7.59</u> 7.65	<u>8.42</u> 8.18	<u>12.43</u> 12.48	$C_{27}H_{32}N_3O_3S_2$	0.81
7	44	195	<u>72.44</u> 72.54	<u>8.51</u> 8.93	<u>5.83</u> 5.64	<u>5.38</u> 6.45	$C_{29}H_{36}N_2O_3S$	0.82

Table 1. Physicochemical characteristics of products formed from compound 1

In the ¹H NMR spectra of 2-7, in contrast to the starting compound 1, we have not revealed the CHO signal. At the same time, we revealed signals from hydantoin (2), phenyl-2-thiazole, and dimedone.

The compounds synthesized efficiently inhibit autooxidation of cumene (Fig. 1).

Experiments on cumene oxidation in the presence of 1–6 (60°C, [AIBN] = 2×10^{-2} M), initiated with



Fig. 1. Kinetic curves of cumene autooxidation in the presence of compounds **1–5** at 110°C. (V(O₂)) Oxygen uptake and (τ) reaction time; the same for Fig. 2. [In]₀, M: (*1*') 0 and (*1–5*) 5 × 10^{–5}; numerals at curves are inhibitor nos.; the same for Fig. 2.

azobis(isobutyronitrile) (AIBN), showed that the compounds synthesized actively terminate oxidation chains by reacting with cumylperoxy radicals (Fig. 2).

From the length of the induction period τ_{ind} , we calculated the stoichiometric coefficient of inhibition *f*, equal to the number of oxidation chains terminated on one molecule of inhibitor and its transformation products:

$$f = \tau_{\rm ind} W_{\rm in} / [\rm In]_0,$$

where W_{in} is the initiation rate, and $[In]_0$ is the initial inhibitor concentration.

From the kinetic curves of the oxygen uptake, we calculated the rate constant of the reaction of the inhibitors with peroxy radicals, k_7 [1, 2]. To this end, the kinetic curves were transformed from the coordinates $V(O_2)-\tau$ to the coordinates $[O_2]^{-1}-\tau^{-1}$, and k_7 was found from the slope of the straight line [2, 3],

$$\tan \alpha = f k_7 [\text{In}]_0 / (k_2 [\text{RH}] W_{\text{in}})$$

where k_2 is the chain initiation constant [2, 3], equal to 1.51 l mol⁻¹ s⁻¹, and [RH] = 7.17 M.

The kinetic parameters of the reactions of compounds **1–5** and **7** with cumylperoxy radicals {f, k_7 (60°C, [AIBN] = 2 × 10⁻² M)} and of cumyl hydroperoxide decomposition [k, v (110°C)] are given in Table 2. As can be seen, k_7 varies within 1.6–4.09 l⁻¹ mol⁻¹ s⁻¹ (with electrondonor substituents, it is higher than with electron-acceptor substituents). As for f, it varies in the range 1.2–2.16.

14010 21			$T = 60^{\circ}C$	T = 1109C		T = 1100C	
Compd.	Formula	$I = 60^{\circ} \text{C}$		$I = 110^{\circ} \text{C}$		$I = 110^{\circ} \text{C}$	
		f	$k_7 \times 10^{-4}$, l mol ⁻¹ s ⁻¹	$k, 1 \text{ mol}^{-1} \text{ s}^{-1}$	ν	$[\ln]_0, M$	τ , min
2	$\begin{array}{c} OH \\ \swarrow \\ OC \\ H \\ CH \\ CH \\ CH \\ S \\ C \\ C$	1.3	1.6	18.5	20000	5 × 10-5	90
3	$\begin{array}{c} OH \\ \swarrow \\ CH = N \\ S \end{array} \begin{array}{c} C_{6}H_{5} \\ C_{6}H_{5} \end{array}$	1.2	4.09	40	45000	5 × 10-5	100
4	$S = C \xrightarrow{NH - CH}_{NH - CH}_{NH - CH}$	2.16	3.8	33	30000	5 × 10-5	180
5	S = C NH - CH NH - CH NH - CH NH - CH OH	1.56	3.94	35	40000	5 × 10 ⁻⁵	130
7	C ₆ H ₅ NH-CH-CH COCH ₃ COCH ₃ COCH ₃	1.8	1.72	28	20000	5 × 10-5	150

 Table 2. Kinetic parameters of reactions of compounds 2–5 and 7



Fig. 2. Kinetic curves of initiated cumene oxidation in the presence of compounds 1–5.

The reactions of 1–6 with cumyl hydroperoxide (CHP) were performed in chlorobenzene under nitrogen at 110°C. All the compounds tested decompose CHP. As demonstrated by the example of inhibitor 1 (Fig. 3), the kinetic curve of CHP decomposition under the action of the compounds tested is S-shaped, which is characteristic of an autocatalytic process. Initially there is certain induction period when the CHP consumption is insignificant, then it is followed by rapid catalytic decomposition, after which the reaction rate decreases because of a decrease in the CHP concentration.

Probably, the inhibitor first reacts with CHP, and then the transformation product formed catalytically decomposes CHP.

To determine the reaction stoichiometry, CHP was



Fig. 3. Kinetic curve of CHP (ROOH) decomposition in the presence of compounds 1. 110°C; $[In]_0 = 1 \times 10^{-4}$, $[ROOH]_0 = 0.26$ M. (τ) Time.

taken in excess. The catalytic factor v characterizes the number of CHP molecules decomposed by one inhibitor molecule. It was calculated by the formula

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

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

Experiments showed that one molecule of 1–5 and 7 is capable to decompose tens of thousands of CHP molecules (Table 2).

EXPERIMENTAL

The ¹H and ¹³C NMR spectra were recorded with a Bruker-300 spectrometer (300 MHz) of the Avance system. The IR spectra were taken with a Specord 75-IR spectrometer from mulls in mineral oil. Thin-layer chromatography of **1–5** and **7** was performed with Silufol UV-254 plates, using 1 : 1 isopropanol–hexane mixture as eluent.

Isopropylbenzene (cumene) (MW 120.2, T_b 152°C, $d_{29.3}$ 862 kg m⁻³, $n_D^{29.3}$ 1.49146) was washed, dried, and distilled under reduced pressure. The cumene purity was checked kinetically, by AIBN-initiated oxidation at 333 K, using a manometric installation [8].

Cumyl hydroperoxide (MW 152, T_b 53°C/13.3 Pa, $d_{29.3}$ 1062 kg m⁻³, $n_D^{29.3}$ 1.5240). Technical-grade cumyl hydroperoxide was shaken with freshly calcined alumina with two- or threefold adsorbent replacement. The precipitate was filtered off, after which CHP was vacuumdistilled twice at 13.3 Pa. Its purity was monitored by the refractive index, density, and available oxygen content determined by iodometric titration [9].

3,5-Di-*tert***-butyl-4-hydroxybenzaldehyde (1).** To a solution of 17.5 g of boric acid and 12.5 g of hexamethylenetetramine in 75 ml of ethylene glycol, heated to 130°C, we added dropwise 9 g of 2,6-di-*tert*-butylphenol. The reaction mixture was stirred for 180 min at 130–135°C, after which 75 ml of dilute (30%) sulfuric acid was slowly added. The oil precipitated in the process crystallizes on cooling. The crystals were washed with cold ethanol and filtered off. White crystals, yield 70%, $R_{\rm f} = 0.93$, eluent isopropanol–hexane (1 : 1), $T_{\rm m}$ 185–186°C (published data [10]: $T_{\rm m}$ 185–186°C).

2,6-Di-*tert*-**butyl-4-**[(**4**-**phenylthiazol-2-ylimino**) **methyl]phenol (3).** A three-necked flask equipped with a water-separating column, a reflux condenser, a thermometer, and a glass stirrer was charged with 7.2 g (0.03 mol) of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (1), 5.28 g (0.03 mol) of 2-amino-4-phenylthiazole, and 20 ml of methanol. The mixture was stirred for 4 h at 60–65°C. To remove the released water completely, a small amount of benzene was added to the reaction mixture. Yellow crystals were obtained; yield 10.2 g (83%), R_f 0.45, eluent isobutanol–decane (1 : 5), T_m 103–104°C. Found, %: C 73.63, H 7.35, N 7.28, S 8.04. C₂₄H₂₈N₂OS. Calculated, %: C 73.43, H 7.19, N 7.14, S 8.17.

4,6-Bis(3,5-di-*tert*-**butyl-4-hydroxyphenyl)hexahydro-1,3,5-triazine-2-thione (4).** A three-necked flask was charged with 2.34 g (0.01 mol) of 3,5-di-*tert*butyl-4-hydroxybenzaldehyde (1), 0.76 g (0.01 mol) of thiourea, and 1.24 ml (0.01 mol) of methylamine. The mixture was left in a fume hood for 7 days at room temperature with continuous stirring. The reaction mixture color gradually changed from white to yellow. Yellow crystals were obtained; yield 1.25 g (35%), $T_{\rm m}$ 147–148°C, $R_{\rm f}$ 0.45, eluent isobutanol–decane (3 : 5). Found, %: C 70.98, H 8.85, N 7.72, S 6.28. C₃₁H₄₇N₃O₂S. Calculated, %: C 70.81, H 9.01, N 7.99, O 6.09, S 6.10.

4,6-Bis(3,5-di-*tert***-butyl-4-hydroxyphenyl)-5-(2-hydroxyethyl)hexahydro-1,3,5-triazine-2-thione (5).** A three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer was charged with the following reactants (0.025 mol each): 5.8 g of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (1), 1.9 g of thiourea, and 1.4 ml of ethanolamine, and also with 20 ml of benzene. The mixture was stirred for 2 days at 72°C. Yellow crys-

tals were obtained; yield 3.4 g (46%), $T_{\rm m}$ 130–131°C, $R_{\rm f}$ 0.71, eluent isopropanol. Found, %: C 69.81, H 8.54, N 7.66, S 5.43. C₃₃H₄₇N₃O₃S. Calculated, %: C 70.05, H 8.37, N 7.43, O 8.48, S 5.67.

5-[4-Phenylthiazol-2-ylamino(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl]thiazolidine-2,4-dione (6). A three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer was charged with 2.34 g (0.01 mol) of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (1), 1.76 g (0.01 mol) of phenylthiazolamine, 1.17 g (0.01 mol) of thiazolidine-2,4-dione, and 20 ml of n-buta-nol. The mixture was stirred for 2 days at 115–120°C. The orange crystals obtained were washed with hexane; yield 21%, T_m 132–133°C, R_f 0.81, eluent isopropanol. Found, %: C 63.27, H 6.59, N 8.42, S 12.43. C₂₇H₃₂N₃O₃S. Calculated, %: C 63.50, H 6.32, N 8.23, O 9.40, S 12.56.

3-[4-Phenylthiazol-2-ylamino(3,5-di-*tert***-butyl-4-hydroxyphenyl)methyl]pentane-2,4-dione (7).** A three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer was charged with 2.34 g (0.01 mol) of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (1), 1.76 g (0.01 mol) of 2-amino-4-phenylthiazole, 10.8 ml (0.01 mol) of acetylacetone, and 20 ml of n-butanol. The mixture was stirred for 6 h at 115–116°C. The yellow crystals obtained were washed with dichloromethane; yield 44%, $T_{\rm m}$ 195°C, $R_{\rm f}$ 0.82, eluent isopropanol–decane (1 : 5). Found, %: C 70.44, H 7.51, N 5.83, S 6.38. C₂₉H₃₆N₂O₃S. Calculated, %: C 70.70, H 7.37, N 5.69, O 9.74, S 6.51.

CONCLUSIONS

(1) A series of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde derivatives were prepared. With hydantoin, C hydantoin-substituted 2,6-di-*tert*-butylphenol was obtained in 86% yield.

(2) Ternary condensation of 3,5-di-*tert*-butyl-4hydroxybenzaldehyde, thiourea, and various amines was performed, and the corresponding 2,6-bis(3,5-di-*tert*-butyl-4-hydroxyphenyl)hexahydro-1,3,5-triazine-4-thiones were obtained.

(3) 3,5-Di-*tert*-butyl-4-hydroxybenzaldehyde derivatives react with cumylperoxy radicals and thus actively terminate oxidation chains.

REFERENCES

1. Ershov, V.V., Nikiforov, T.A., and Volod'kin, A.A., *Prostranstvenno-zatrudnennye fenoly* (Sterically Hindered Phenols), Moscow: Khimiya, 1972.

- 2. Rzaeva, I.A., Sadigova, S.E., Vekilova, T.M., et al., *Neftekhimiya*, 2005, vol. 45, no. 6, pp. 470–475.
- 3. Farzaliev, V.M., Allakhverdiev, M.A., Magerramov, A.M., et al., *Zh. Prikl. Khim.*, 2001, vol. 74, no. 1, pp. 110–113.
- Farzaliev, V.M., Allakhverdiev, M.A., Sattar-zade, R.I., and Rzaeva, I.A., *Zh. Prikl. Khim.*, 2001, vol. 74, no. 12, pp. 2023–2026.
- Farzaliev, V.M., Magerramov, A.M., Bairamov, M.R., et al., *Zh. Prikl. Khim.*, 2008, vol. 81, no. 1, pp. 78–81.
- Allakhverdiev, M.A., Babai, R.M., Farzaliev, V.M., et al., *Neftekhimiya*, 2001, vol. 41, no. 2, pp. 153–157.

- Silverstein, R.M., Bassler, G.C., and Morrill, T.C., Spectrometric Identification of Organic Compounds, New York: Wiley, 1974, 3rd ed.
- Weissberger, A. and Proskauer, E.S., Organic Solvents. *Physical Properties and Methods of Purification*, Riddick, J.A. and Toops, E.E., Eds., New York: Interscience, 1955.
- 9. Antonovskii, V.L., Organicheskie perekisnye initsiatory (Organic Peroxide Initiators), Moscow: Khimiya, 1972.
- Nikiforov, G.A., Dyumaev, K.M., Volod'kin, A.A., and Ershov, V.V., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1962, pp. 1836–1838.