Synthesis and inhibitory activity of alkyl(hydroxyaryl)amines*

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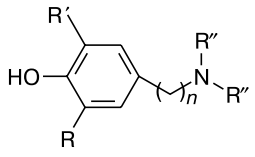
The reaction of ω-(4-hydroxyaryl)haloalkanes with various nitrogen-containing agents afforded primary, secondary, and tertiary amino derivatives of 2,6-dialkylphenols. For the compounds synthesized, the reaction rate constants with peroxide radicals were measured for cumene and methyl oleate oxidation. The total inhibitory activity in the model reactions of thermal autooxidation of lard and hexadecane was studied. The rate constants of alkyl(hydroxylaryl)amines are the same as those of the corresponding alkylphenols, whereas the total inhibitory activity of some alkyl(hydroxylaryl)amines exceeds substantially that for alkylphenols.

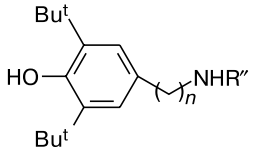
Key words: 2,6-dialkylphenols, ω-(4-hydroxyaryl)haloalkanes, alkyl(hydroxylaryl)amines, aminoalkylphenols, antioxidation activity, peroxide radicals, total inhibitory activity.

Alkyl(hydroxyaryl)amines (aminoalkylphenols) are highly efficient inhibitors for free radical oxidation of various organic substrates. According to patent data,[1—4] they can be used as stabilizers of polymeric materials, rubbers, lubricants, and diesel and jet fuels. In addition, alkyl(hydroxyaryl)amines and their salts possess a high spectrum of biological activity, in particular, they manifest antiphlogistic,[5] antiarrhythmic,[6] radioprotective, and antitumor[7] properties. At the same time, regularities of changes in the antioxidation activity of alkyl(hydroxyaryl)amines depending on their structure are insufficiently studied: these data are presented only in few studies[8—12] devoted predominantly to benzylic compounds.

In the present study, we synthesized structurally related series of alkyl(hydroxyaryl)amines **1**—**6** and studied comparatively their antioxidation activity in various model systems.



1a—i, **2a—f**, **3a—d**



4a—c—6a—c

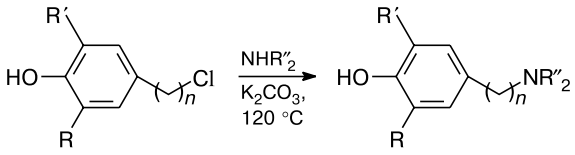
R = R´ = Bu^t, *n* = 2 (**a**), 3 (**b**), 4 (**c**); R = Bu^t, R´ = H, *n* = 3 (**d**);
R = R´ = Me, *n* = 3 (**e**); R = R´ = H, *n* = 3 (**f**);
R = R´ = *cyclo*-C_6H_{11}, *n* = 3 (**g**); R = Bu^t, R´ = Me, *n* = 3 (**h**);
R = R´ = Bu^t, *n* = 5 (**i**)
R″ = Me (**1a—i**, **4a—c**), Et (**2a—f**), Pr (**3a—d**, **5a—c**), H (**6a—c**)

* Dedicated to the memory of Academician N. N. Vorozhtsov on the 100th anniversary of his birth.

Results and Discussion

Tertiary amines **1**—**3** were synthesized by the reactions of the corresponding ω-(4-hydroxyaryl)chloroalkanes **7** with dialkylamines in yields up to 90% (Scheme 1).

Scheme 1



7a—i **1a—i**, **2a—f**, **3a—d**

7: R = R´ = Bu^t, *n* = 2 (**a**), 3 (**b**), 4 (**c**); R = Bu^t, R´ = H, *n* = 3 (**d**);
R = R´ = Me, *n* = 3 (**e**); R = R´ = H, *n* = 3 (**f**);
R = R´ = *cyclo*-C_6H_{11}, *n* = 3 (**g**); R = Bu^t, R´ = Me, *n* = 3 (**h**);
R = R´ = Bu^t, *n* = 5 (**i**)

Secondary amines **4a**—**c** and **5a**—**c** were synthesized similarly in 60—72% yields by the reactions of chloroalkanes **7** with methyl- and propylamines.

Primary amines **6a**—**c** were synthesized from bromoalkanes **8a**—**c** through intermediate alkylphthalimides **9a**—**c** (Scheme 2).

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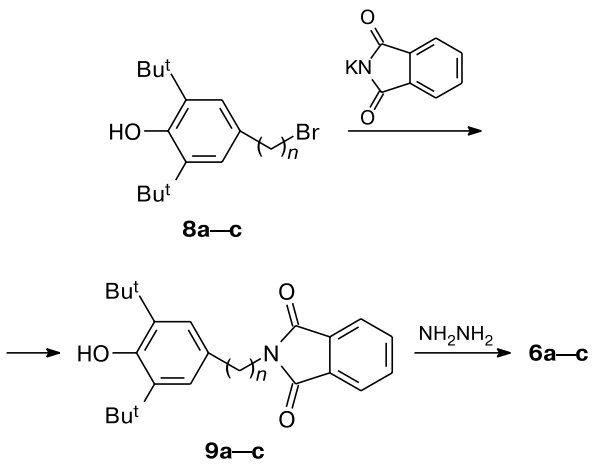
Scheme 2



n = 2 (**a**), 3 (**b**), 4 (**c**)

The compositions and structures of aminoalkylphenols **1**—**6** synthesized were confirmed by elemental analysis data and spectral characteristics.

Aminoalkylphenols **1**—**6** contain two functional groups, namely, the phenol and alkylamine groups, capable of inhibiting processes of free radical oxidation. The phenolic OH group acts as an inactivator of active radicals, and the alkylamine group can decompose peroxides to form *N*-oxides[11] or regenerate phenol due to the aminoperoxide radicals formed by oxidation.[13]

The antiradical activity of the phenol fragments of compounds **1**—**6** was studied under the conditions of cumene and methyl oleate oxidation initiated by AIBN. The total inhibitory activity was determined for the thermal autooxidation of hexadecane and lard.

Earlier[12] synthesized dimethyl(3-R^1-5-R^2-4-hydroxybenzyl)amines **10a**—**d** (R^1 = R^2 = Bu^t (**a**); R^1 = Bu^t, R^2 = Me (**b**); R^1 = R^2 = Me (**c**); R^1 = R^2 = *cyclo*-C_6H_{11} (**d**)), 2,6-di-*tert*-butyl-4-methylphenol (ionol), 2-*tert*-butyl-4-methylphenol (TBMP), 2,4,6-trimethylphenol (TMP), 2,6-dicyclohexyl-4-methylphenol (DCHMP), and 4-methylphenol (MP) were used as reference antioxidants.

The antiradical activity of the compounds studied was characterized by the rate constants of their reactions with the peroxide radicals of cumene and methyl oleate (k).

$$ArOH + ROO^{\cdot} \xrightarrow{k} ArO^{\cdot} + ROOH$$

The initial regions of the kinetic curves of oxygen absorption for AIBN-initiated cumene and methyl oleate oxidation in the presence of the compounds under study (Figs 1 and 2) are well linearized in the coordinates of the equation

$$\Delta[O_2]/RH = -k_1/k\ln(1 - t/\tau), \qquad (1)$$

where $\Delta[O_2]$ is the amount of absorbed oxygen referred to the sample volume; k and k_1 are the reaction rate constants of the peroxide radicals with molecules of the inhibitor and oxidized substrate, respectively; τ is the induction period; t is time; [RH] is the substrate concentration in the sample.

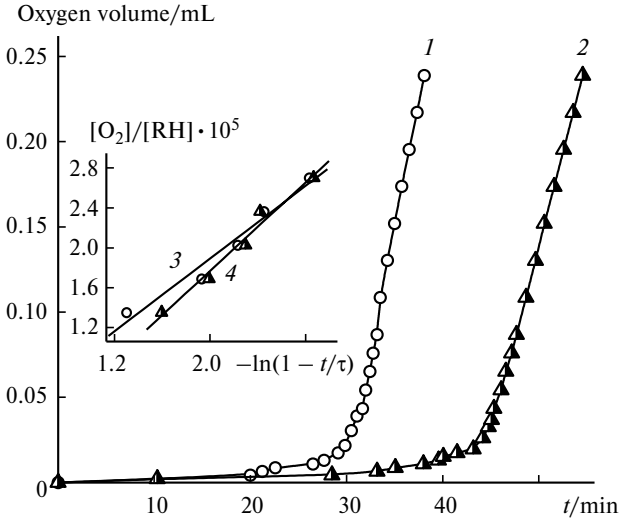


Fig. 1. Kinetic curves of oxygen absorption in initiated cumene oxidation at 60 °C in the presence of TMP (*1*) and amine **1i** (*2*); their anamorphoses are given in inset (*3* and *4*, respectively).

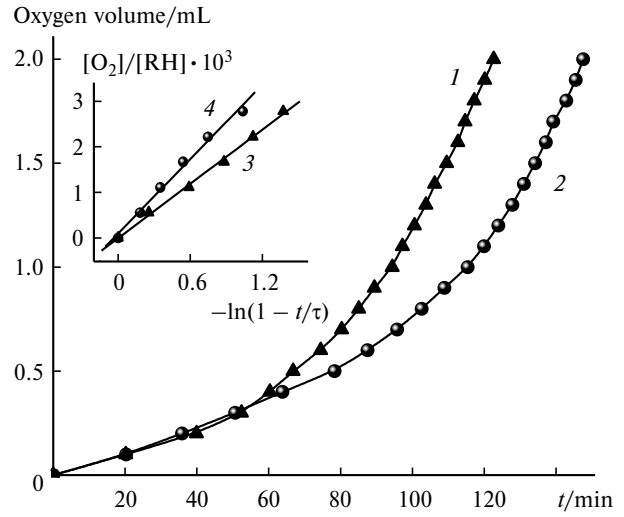


Fig. 2. Kinetic curves of oxygen absorption in initiated methyl oleate oxidation in chlorobenzene at 60 °C in the presence of amine **1g** (*1*) and ionol (*2*); their anamorphoses are given in inset (*3* and *4*, respectively).

This indicates that the reactions of cumene and methyl oleate oxidation are inhibited according to the commonly accepted scheme[14] and the k rate constant can be determined by Eq. (1).

The k_1/k ratio was determined from the slope ratios of the straight lines in the coordinates of the plot of $\Delta[O_2]/[RH]$ *vs.* $-\ln(1 - t/\tau)$. The absolute values of the k constant for cumene oxidation were calculated using

Table 1. Parameters of the antioxidation activity of 2-R^1-4-R^2-6-R^3-substituted phenols

Compound	R^1	R^2	R^3	$k \cdot 10^{-4}$/L mol^{-1} s^{-1}		τ/min	
				Cumene	Methyl oleate	Hexadecane	Lard
1a	Bu^t	$(CH_2)_2NMe_2$	Bu^t	2.5±0.3	2.6±0.2	139±5	288±5
1b	Bu^t	$(CH_2)_3NMe_2$	Bu^t	2.5±0.3	3.0±0.2	135±7	334±5
1c	Bu^t	$(CH_2)_4NMe_2$	Bu^t	2.4±0.2	2.9±0.2	142±5	435±5
1d	H	$(CH_2)_3NMe_2$	Bu^t	9.6±0.2	1.4±0.2	111±5	143±5
1e	Me	$(CH_2)_3NMe_2$	Me	13.8±3.0	3.4±0.1	76±5	123±5
1f	H	$(CH_2)_3NMe_2$	H	1.7±0.2	—	7±2	51±5
1g	*cyclo*-C_6H_{11}	$(CH_2)_3NMe_2$	*cyclo*-C_6H_{11}	11.4±2.0	3.8±0.2	72±5	143±6
1h	Bu^t	$(CH_2)_3NMe_2$	Me	13.7±3.3	4.0±0.3	106±5	245±5
1i	Bu^t	$(CH_2)_5NMe_2$	Bu^t	—	—	130±5	470±5
2b	Bu^t	$(CH_2)_3NEt_2$	Bu^t	2.3±0.3	2.4±0.2	88±5	307±5
3b	Bu^t	$(CH_2)_3NPr_2$	Bu^t	2.0±0.4	2.3±0.2	63±5	277±6
4b	Bu^t	$(CH_2)_3NHMe$	Bu^t	2.7±0.3	2.9±0.2	92±5	234±5
6b	Bu^t	$(CH_2)_3NH_2$	Bu^t	2.5±0.3	3.0±0.2	87±5	254±8
10a	Bu^t	CH_2NMe_2	Bu^t	2.0±0.4	2.2±0.2	119±5	110±5
10b	Bu^t	CH_2NMe_2	Me	11.6±1.0	4.2±0.5	97±5	150±5
10c	Me	CH_2NMe_2	Me	14.6±3.3	3.8±1.0	76±5	122±5
10d	*cyclo*-C_6H_{11}	CH_2NMe_2	*cyclo*-C_6H_{11}	18.1±3.0	5.1±0.3	71±5	130±5
MP	H	Me	H	1.5±0.2	—	7±2	15±2
Ionol	Bu^t	Me	Bu^t	2.2±0.6	2.6±0.4	80±5	165±5
TMP	Me	Me	Me	10.4±1.2	3.6±0.3	78±5	75±5
DCHMP	*cyclo*-C_6H_{11}	Me	*cyclo*-C_6H_{11}	11.7±5.8	4.7±0.2	80±5	108±5
TBMP	Bu^t	Me	H	9.3±0.2	2.0±0.2	85±5	78±5

Note. The induction period for noninhibited lard is 15 min and that for hexadecane is 7 min.

the known[15] k_1 value (1.75 L mol^{-1} s^{-1}). For the oxidation of methyl oleate in chlorobenzene, the k_1 value (60.8 L mol^{-1} s^{-1}) was estimated from the known k value for ionol ($2.6 \cdot 10^4$ L mol^{-1} s^{-1}).[16] The k constants found by us (with the root-mean-square deviation) are presented in Table 1.

It was shown for the 2,6-di-*tert*-butyl-substituted derivatives that the compounds bearing different alkylamine groups (NMe_2, NEt_2, NPr_2, NHMe, and NH_2) and containing the nitrogen atom remote from the aromatic ring at different distances are characterized in cumene and methyl oleate oxidation by similar k rate constant values close to the value for ionol.

At the same time, variations in the number and structure of the substituents in the *ortho*-position of the phenolic fragment were accompanied by changes in the k rate constant values. For the oxidation of both cumene and methyl oleate, the replacement of the *tert*-butyl substituents in the *ortho*-position by the methyl and cyclohexyl groups in molecules of the compounds under study increased the k constant.

It is found that in both model systems the di-*tert*-butyl-substituted derivatives are characterized by close k values ($(2.0—3.0) \cdot 10^4$ L mol^{-1} s^{-1}), whereas for less shielded 2,6-dialkylphenols the k value for cumene oxidation took higher values ($(1.1—1.8) \cdot 10^5$ L mol^{-1} s^{-1}) than that for methyl oleate oxidation ($(3.4—5.1) \cdot 10^4$ L mol^{-1} s^{-1}).

The lower k rate constant values for the di-*tert*-butyl-substituted derivatives are due, evidently, to the steric factor. It is most likely that the reactivity of *ortho*-disubstituted amines **1e**,**g**,**h** and **10b—d**, TMP, and DCHMP in methyl oleate oxidation decreases because of hydrogen bonding between the OH groups of the antioxidant molecules and ester groups of the methyl oleate molecules.[17]

For cumene oxidation, the k constant value in the series **1b—1d—1f** and ionol—TBMP—MP changes nonmonotonically: it increases on going from di-*tert*-butyl- to mono-*tert*-butyl-substituted phenols and decreases on going from the latter to *ortho*-substituted phenols. This fact can be due to the dual effect of the *ortho*-*tert*-butyl substituents on the reactivity of phenols in the reaction with peroxide radicals.[14] On the one hand, these substituents decrease the energy of the ArO—H bond cleaved in the reaction. On the other hand, they create steric hindrance for the interaction of the phenolic OH group with the active radical. As a consequence, the intermediate mono-*tert*-butyl substitution to the *ortho*-position is most "favorable."

The antiradical activity decreased for the oxidation of methyl oleate in the series of compounds **1b—1d—1f** and ionol—TBMP—MP. In this model system, *ortho*-substi-

tuted amine **1f** and MP exerted virtually no inhibition effect on methyl oleate oxidation.

According to the obtained data, aminoalkylphenols synthesized exerted a pronounced inhibition effect on the thermal oxidation of lard and hexadecane (see Table 1). They increased the thermooxidation stability of these substrates by 3.4—30 times, and the series of aminoalkylphenols inhibited the oxidation process much more efficiently than the corresponding alkylphenols, which is associated, most likely, with the bifunctional mechanism of their antioxidation effect.[11]

The ability of aminoalkylphenols to inhibit lard and hexadecane oxidation was found to be determined, to a great extent, by the structure of their molecules: the structure of the substituents at the nitrogen atom, the alkyl chain length separating the phenol and alkylamine groups, and the number and structure of the substituents in the *ortho*-position.

It is shown that tertiary amine **1b** has the highest antioxidation activity in the oxidation of both lard and hexadecane in the series of di-*tert*-butyl-substituted aminoalkylphenols **1b**—**4b**—**6b** bearing the nitrogen atom with different numbers of alkyl substituents. The inhibitory activity of tertiary amines, in turn, decreased on going from *N*,*N*-dimethyl-substituted amine **1b** to its *N*,*N*-diethyl- and *N*,*N*-dipropyl-substituted analogs (**2b** and **3b**, respectively).

The inhibitory activity of 2,6-di-*tert*-butyl-substituted *p*-aminoalkylphenols **1a**—**c**,**i** and **10a** containing different carbon atoms in the alkyl chain for lard oxidation increased with removing the nitrogen atom from the aromatic ring. Among the compounds mentioned, the highest antioxidant activity belongs to amine **1i**, in which the amino group is remote from the aromatic ring by five methylene units. No distinct relation between the alkyl chain length in the *para*-position and antioxidant activity of these compounds was observed for hexadecane oxidation.

For the oxidation of lard and hexadecane in the series of amines **1b**—**1d**—**1f** and **1b**—**1h**—**1e**—**1g**, the antioxidation activity decreased with a decrease in the number of the *ortho*-*tert*-butyl substituents and with their substitution for the methyl and cyclohexyl groups, *i.e.*, with a decrease in the degree of steric shielding of the phenolic OH group. For the oxidation of hexadecane in the series of hydroxybenzylamines **10a**—**d**, a similar change in the antioxidation activity was observed, depending on the structure of substituents in the *ortho*-position, whereas benzylamine **10b** with the "intermediate" methyl-*tert*-butyl *ortho*-substitution was most efficient for lard oxidation.

As a whole, the results of the present studies indicate that in the series of the compounds synthesized the highest total inhibitory activity belongs to *N*,*N*-dimethyl-alkyl-ω-(3,5-di-*tert*-butyl-4-hydroxyaryl)amines **1a**—**c**,**i**, in which the nitrogen atom is separated from the aromatic ring by two—five methylene units. These amines are of interest for further investigation as potential antioxidants used in practice.

Experimental

ω-(4-Hydroxyaryl)haloalkanes synthesized according to earlier described methods[18—20] were used as the starting synthons for the preparation of aminoalkylphenols **1**—**6**.

^{1}H NMR spectra were recorded on a Bruker DRX500 spectrometer with a working frequency of 500.13 MHz, $CDCl_3$ as the solvent, and $CHCl_3$ as the standard (δ 7.24). Melting points were determined in a capillary on a PTP instrument (Industrial Complex PO Khimlaborpribor, Russia).

The synthesis and characteristics of tertiary alkyl(hydroxyaryl)amines **1a**—**d**,**f**,**g**, **2a**—**c**,**f**, and **3b** and secondary amine **4b** have been described previously.[11,21]

Alkylphthalimide **9b** and propylamine **6b** were synthesized according to a known procedure.[21]

***N*,*N*-Dimethyl-5-(3,5-di-*tert*-butyl-4-hydroxyphenyl)pentylamine (1i).** 1-Chloro-5-(3,5-di-*tert*-butyl-4-hydroxyphenyl)pentane (2.3 g, 7.4 mmol), dimethylamine (2.0 g, 14.8 mmol), and potassium carbonate (2.1 g, 14.8 mmol) were placed in a 50-mL ampule, and ethanol (10 mL) was added. The ampule was sealed, placed in a thermostat with a shaking device, and stored for 7 h at 120 °C. After cooling, the ampule was opened, and the reaction mixture was treated with an aqueous solution of NaOH and then toluene. The extract was washed with water and dried over Na_2SO_4, and the solvent was distilled off. The residue was distilled *in vacuo*, and amine **1i** (1.8 g, 76%) was obtained, b.p. 148—150 °C (1 Torr), m.p. 91—92 °C (from hexane). Found (%): C, 79.07; H, 11.89; N, 4.14. $C_{21}H_{37}NO$. Calculated (%): C, 78.94; H, 11.67; N, 4.38. ^{1}H NMR, δ: 1.36 (m, 2 H, $Ar(CH_2)_2C\underline{H}_2$); 1.42 (s, 18 H, Bu^t); 1.50 (m, 2 H $Ar(CH_2)_3C\underline{H}_2$); 1.60 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.20 (s, 6 H, NMe_2); 2.25 (t, 2 H, CH_2N, J = 7.5 Hz); 2.50 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 5.01 (s, 1 H, OH); 6.96 (s, 2 H, Ar).

Compounds **1e**,**h**, **2d**,**e**, and **3a**,**c**,**d** were synthesized similarly from the corresponding haloalkanes.

***N*,*N*-Dimethyl-3-(4-hydroxy-3,5-dimethylphenyl)propylamine (1e).** The yield was 72%, b.p. 125—127 °C (1 Torr), m.p. 53.5—54 °C (from hexane). Found (%): C, 75.46; H, 10.40; N, 6.48. $C_{13}H_{21}NO$. Calculated (%): C, 75.31; H, 10.21; N, 6.76. ^{1}H NMR, δ: 1.68—1.75 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.20 (s, 6 H, $Ar\underline{Me}$); 2.10 (s, 6 H, NMe_2); 2.27 (t, 2 H, CH_2N, J = 7.5 Hz); 2.47 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 5.43 (s, 1 H, OH); 6.76 (s, 2 H, Ar).

***N*,*N*-Dimethyl-3-(5-*tert*-butyl-4-hydroxy-3-methylphenyl)propylamine (1h).** The yield was 72%, b.p. 129—131 °C (1 Torr), m.p. 79—80 °C (from hexane). Found (%): C, 77.22; H, 11.05; N, 5.48. $C_{16}H_{27}NO$. Calculated (%): C, 77.06; H, 10.91; N, 5.62. ^{1}H NMR, δ: 1.39 (s, 9 H, Bu^t); 1.69—1.76 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.19 (s, 3 H, $Ar\underline{Me}$); 2.22 (s, 6 H, NMe_2); 2.28 (t, 2 H, CH_2N, J = 7.5 Hz); 2.50 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 5.00 (s, 1 H, OH); 6.80 (d, 1 H, Ar, J = 1.5 Hz); 6.93 (d, 1 H, Ar, J = 2.5 Hz).

***N*,*N*-Diethyl-3-(3-*tert*-butyl-4-hydroxyphenyl)propylamine (2d).** The yield was 90%, b.p. 145—147 °C (2 Torr). Found (%): C, 77.74; H, 11.25; N, 5.00. $C_{17}H_{29}NO$. Calculated (%): C, 77.51; H, 11.10; N, 5.32. ^{1}H NMR, δ: 1.04 (t, 6 H,

$N(CH_2C\underline{H}_3)_2$, J = 7.5 Hz); 1.45 (s, 9 H, Bu^t); 1.80 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.49 (t, 2 H, $C\underline{H}_2NEt_2$, J = 7.5 Hz); 2.53 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 2.64 (q, 4 H, $N(C\underline{H}_2CH_3)_2$); 6.00 (br.s, 1 H, OH); 6.48 (d, 1 H, Ar, J = 8 Hz); 6.78 (dd, 1 H, Ar, J = 8 Hz, J = 2 Hz); 7.01 (d, 1 H, Ar, J = 2 Hz).

***N,N*-Diethyl-3-(4-hydroxy-3,5-dimethylphenyl)propylamine (2e).** The yield was 90%, b.p. 145—147 °C (1 Torr). Found (%): C, 76.78; H, 10.94; N, 5.64. $C_{15}H_{25}NO$. Calculated (%): C, 76.55; H, 10.71; N, 5.95. ^{1}H NMR, δ: 0.96 (t, 6 H, $N(CH_2C\underline{H}_3)_2$, J = 7.5 Hz); 1.65—1.72 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.20 (s, 6 H, Me); 2.42—2.47 (m, 4 H, $ArC\underline{H}_2CH_2C\underline{H}_2$); 2.51—2.55 (q, 4 H, $N(C\underline{H}_2CH_3)_2$); 4.80 (s, 1 H, OH); 6.76 (s, 2 H, Ar).

***N,N*-Dipropyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethylamine (3a).** The yield was 83%, b.p. 148—150 °C (2 Torr). Found (%): C, 79.41; H, 11.85; N, 3.96. $C_{22}H_{39}NO$. Calculated (%): C, 79.22; H, 11.79; N, 4.20. ^{1}H NMR, δ: 0.92 (t, 6 H, $N(CH_2CH_2C\underline{H}_3)_2$, J = 7.5 Hz); 1.49 (s, 18 H, Bu^t); 1.51 (m, 4 H, $N(CH_2C\underline{H}_2CH_3)_2$); 2.45 (t, 4 H, $N(C\underline{H}_2CH_2CH_3)_2$, J = 7.5 Hz); 2.65 (m, 4 H, $ArC\underline{H}_2C\underline{H}_2$); 4.94 (s, 1 H, OH); 6.94 (s, 2 H, Ar).

***N,N*-Dipropyl-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)butylamine (3c).** The yield was 73%, b.p. 165—166 °C (1 Torr). Found (%): C, 79.94; H, 12.04; N, 3.55. $C_{24}H_{43}NO$. Calculated (%): C, 79.72; H, 11.99; N, 3.87. ^{1}H NMR, δ: 0.90 (t, 6 H, $N(CH_2CH_2C\underline{H}_3)_2$, J = 7.5 Hz); 1.43 (m, 4 H, $N(CH_2C\underline{H}_2CH_3)_2$); 1.46 (s, 18 H, Bu^t); 1.49 (m, 2 H, $Ar(CH_2)_2C\underline{H}_2$); 1.60 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.35 (t, 4 H, $N(C\underline{H}_2Et)_2$, J = 7.5 Hz); 2.42 (t, 2 H, $C\underline{H}_2NPr_2$, J = 7.5 Hz); 2.53 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 4.89 (s, 1 H, OH); 6.89 (s, 2 H, Ar).

***N,N*-Dipropyl-3-(3-*tert*-butyl-4-hydroxyphenyl)propylamine (3d).** The yield was 62%, b.p. 152—153 °C (1 Torr), m.p. 74—75 °C (from hexane). Found (%): C, 78.31; H, 11.59; N, 4.67. $C_{19}H_{33}NO$. Calculated (%): C, 78.29; H, 11.41; N, 4.81. ^{1}H NMR, δ: 0.88 (t, 6 H, $N(CH_2CH_2C\underline{H}_3)_2$, J = 7.5 Hz); 1.39 (s, 9 H, Bu^t); 1.46 (m, 4 H, $N(CH_2C\underline{H}_2CH_3)_2$); 1.73 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.38 (t, 4 H, $N(C\underline{H}_2Et)_2$, J = 7.5 Hz); 2.44 (t, 2 H, CH_2N, J = 7.5 Hz); 2.49 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 6.04 (br.s, 1 H, OH); 6.39 (d, 1 H, Ar, J = 8 Hz); 6.78 (dd, 1 H, Ar, J = 8 Hz, J = 2 Hz); 7.01 (d, 1 H, Ar, J = 2 Hz).

***N*-Methyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethylamine (4a).** 1-Chloro-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethane (5.0 g, 18.6 mmol), methylamine (14.8 mL, 0.11 mol), and potassium carbonate (5.1 g, 37.2 mmol) were placed in a 50-mL ampule, and ethanol (10 mL) was added. The ampule was sealed, placed in a thermostat with a shaking device, and stored for 7 h at 120 °C. After cooling the ampule was opened, and the reaction mixture was treated with an aqueous solution of NaOH and then toluene. The extract was washed with water and dried over Na_2SO_4, and the solvent was distilled off. The residue was distilled *in vacuo*, and target amine **4a** was obtained (2.9 g, 60%), b.p. 140—142 °C (1 Torr), m.p. 65—68 °C (from hexane). Found (%): C, 77.38; H, 10.97; N, 5.45. $C_{17}H_{29}NO$. Calculated (%): C, 77.51; H, 11.10; N, 5.32. ^{1}H NMR, δ: 1.42 (s, 18 H, Bu^t); 2.45 (s, 3 H, Me); 2.73 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 2.82 (t, 2 H, $C\underline{H}_2N$, J = 7.5 Hz); 3.03—6.62 (br.s, 2 H, OH, NH); 6.99 (s, 2 H, Ar).

Compounds **4c** and **5a—c** were synthesized similarly.

***N*-Methyl-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)butylamine (4c).** The yield was 72%, b.p. 169—172 °C (1 Torr), m.p. 70—71 °C (from hexane). Found (%): C, 78.44; H, 11.49; N, 4.64. $C_{19}H_{33}NO$. Calculated (%): C, 78.29; H, 11.41; N, 4.81. ^{1}H NMR, δ: 1.44 (s, 18 H, Bu^t); 1.60 (m, 4 H, $ArCH_2C\underline{H}_2C\underline{H}_2$); 2.43 (s, 3 H, Me); 2.55 (t, 2 H, $C\underline{H}_2NHMe$, J = 7.5 Hz); 2.62 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.00—6.00 (br.s, 2 H, OH, NH); 6.97 (s, 2 H, Ar).

***N*-Propyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethylamine (5a).** The yield was 65%, b.p. 136—138 °C (1 Torr), m.p. 33 °C (from hexane). Found (%): C, 78.48; H, 11.57; N, 4.54. $C_{19}H_{33}NO$. Calculated (%): C, 78.29; H, 11.41; N, 4.81. ^{1}H NMR, δ: 0.70—0.80 (br.s, 1 H, NH); 0.89 (t, 3 H, $NCH_2CH_2C\underline{H}_3$, J = 7.5 Hz); 1.45 (s, 18 H, Bu^t); 1.43—1.51 (m, 2 H, $NCH_2C\underline{H}_2CH_3$); 2.56 (t, 2 H, $NC\underline{H}_2CH_2CH_3$, J = 7.5 Hz); 2.64 (t, 2 H, $ArCH_2C\underline{H}_2N$, J = 7.5 Hz); 2.77 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 4.92 (s, 1 H, OH); 6.89 (s, 2 H, Ar).

***N*-Propyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylamine (5b).** The yield was 68%, m.p. 66 °C (from hexane). Found (%): C, 78.88; H, 11.61; N, 4.44. $C_{20}H_{35}NO$. Calculated (%): C, 78.63; H, 11.55; N, 4.59. ^{1}H NMR, δ: 0.65—0.80 (br.s, 1 H, NH); 0.91 (t, 3 H, $NCH_2CH_2C\underline{H}_3$, J = 7.5 Hz); 1.43 (s, 18 H, Bu^t); 1.46—1.49 (m, 2 H, $NCH_2C\underline{H}_2CH_3$); 1.72—1.75 (m, 2 H, $ArCH_2C\underline{H}_2$); 2.50—2.55 (m, 4 H, CH_2NCH_2); 2.60 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 4.90 (s, 1 H, OH); 6.87 (s, 2 H, Ar).

***N*-Propyl-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)butylamine (5c).** The yield was 64%, b.p. 156—158 °C (1 Torr), m.p. 41 °C (from hexane). Found (%): C, 79.15; H, 11.73; N, 4.41. $C_{21}H_{37}NO$. Calculated (%): C, 78.94; H, 11.67; N, 4.38. ^{1}H NMR, δ: 0.65—0.80 (br.s, 1 H, NH); 0.91 (s, 3 H, $NCH_2CH_2C\underline{H}_3$); 1.43 (s, 18 H, Bu^t); 1.47—1.48 (m, 4 H, $ArCH_2(C\underline{H}_2)_2$); 1.50—1.51 (m, 2 H, $NCH_2C\underline{H}_2CH_3$); 2.49 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 2.55 (t, 2 H, $NC\underline{H}_2CH_2CH_3$, J = 7.5 Hz); 2.61 (t, 2 H, $C\underline{H}_2NHPr$, J = 7.5 Hz); 4.85 (br.s, 1 H, OH); 6.86 (s, 2 H, Ar).

2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)ethylphthalimide (9a). A mixture of 1-bromo-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethane (10.1 g, 32.23 mmol), potassium phthalimide (7.2 g, 38.68 mmol), and DMF (50 mL) was heated for 6 h at 120 °C, cooled, and filtered. The filtrate was treated with toluene, the extract was washed with water and dried over Na_2SO_4, the solvent was distilled off, and the residue was recrystallized from ethanol. Alkylphthalimide **9a** was obtained (9.0 g, 63%), m.p. 130—132 °C. Found (%): C, 76.05; H, 7.90; N, 3.47. $C_{24}H_{29}NO_3$. Calculated (%): C, 75.96; H, 7.70; N, 3.69. ^{1}H NMR, δ: 1.38 (s, 18 H, Bu^t); 2.90 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.89 (t, 2 H, CH_2N, J = 7.5 Hz); 5.06 (s, 1 H, OH); 6.99 (s, 2 H, Ar); 7.68, 7.81 (both m, 2 H each, Ar).

4-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)butylphthalimide (9c) was synthesized similarly to phthalimide **9a**. The yield was 68%, m.p. 140—142 °C (from ethanol). Found (%): C, 76.81; H, 8.23; N, 3.25. $C_{26}H_{33}NO_3$. Calculated (%): C, 76.62; H, 8.16; N, 3.44. ^{1}H NMR, δ: 1.47 (s, 18 H, Bu^t); 1.69 (m, 2 H, $ArCH_2C\underline{H}_2$); 1.79 (m, 2 H, $Ar(CH_2)_2C\underline{H}_2$); 2.60 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.77 (t, 2 H, CH_2N, J = 7.5 Hz); 5.07 (s, 1 H, OH); 7.01 (s, 2 H, Ar); 7.74, 7.88 (both m, 2 H each, Ar).

2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)ethylamine (6a). Alkylphthalimide **9a** (3.0 g, 7.91 mmol) was dissolved in ethanol on heating, and an aqueous solution of hydrazine hydrate (3.5 mL, 79.1 mmol) was added. The mixture was refluxed for 2 h and then cooled, a solution of HCl (10 mL, 0.12 mol) was added, and the resulting mixture was stirred for 0.5 h. Then water (50 mL) was added, and the mixture was heated, stirred for 0.5 h

at 80 °C, cooled, and filtered. The filtrate was treated with an aqueous solution of NaOH and then toluene. The extract was washed with water and dried with Na_2SO_4, the solvent was distilled off, and the residue was recrystallized from hexane. Amine **6a** (1.3 g, 68%) was obtained, m.p. 108—110 °C (from hexane) (*cf.* Ref. 22: m.p. 107.0—107.6 °C). Found (%): C, 77.22; H, 11.08; N, 3.47. $C_{16}H_{27}NO$. Calculated (%): C, 77.06; H, 10.91; N, 3.69. ^{1}H NMR, δ: 1.00—1.25 (br.s, 2 H, NH_2); 1.43 (s, 18 H, Bu^t); 2.66 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 2.93 (t, 2 H, CH_2N, J = 7.5 Hz); 4.05—5.81 (br.s, 1 H, OH); 6.98 (s, 2 H, Ar).

4-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)butylamine (6c) was synthesized similarly to amine **6a** from alkylphthalimide **9c**. The yield was 92%, m.p. 71—72 °C (from hexane) (*cf.* Ref. 22: m.p. 71—72 °C). Found (%): C, 78.01; H, 11.45; N, 4.77. $C_{18}H_{31}NO$. Calculated (%): C, 77.92; H, 11.26; N, 5.05. ^{1}H NMR, δ: 1.42 (s, 18 H, Bu^t); 1.42—1.60 (br.s, 2 H, NH_2); 1.48 (m, 2 H, $ArCH_2C\underline{H}_2$); 1.60 (m, 2 H, $Ar(CH_2)_2C\underline{H}_2$); 2.48 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 2.69 (t, 2 H, CH_2NH_2, J = 7.5 Hz); 3.35—6.30 (br.s, 1 H, OH); 6.89 (s, 2 H, Ar).

In the kinetic studies, commercial ionol (Acros Organics), TMP (Lancaster), TBMP (Acros Organics), and MP (Russia) were used. 2,6-Dicyclohexyl-4-methylphenol was synthesized using a known procedure.[23]

The k values were determined in model reactions of the AIBN-initiated oxidation of cumene and methyl oleate (all Acros Organics) in chlorobenzene at 60 °C. Methyl oleate was purified prior to use by double vacuum distillation.

The kinetics of oxygen absorption was studied using a high-sensitive capillary volumeter and a gasometric setup described previously.[15] The induction period (τ) was determined in the plot as an intersection point of two tangents to the kinetic curve. The slope ratios of these tangents were 0.5 and 0.75 of the slope ratio of the straight line corresponding to the noninhibited reaction.[15]

The initiation rate (W_i) was determined by the inhibitor method from the time of the end of the induction period of cumene (methyl oleate) oxidation in the presence of ionol or TMP

$$W_i = 2[ArOH]_0/\tau,$$

where $[ArOH]_0$ is the initial concentration of the inhibitor.

The main experiments on cumene oxidation were carried out at $W_i = (0.2—1.4)\cdot10^{-7}$ mol L^{-1} s^{-1} and [ArOH] = $(2.5—3.3)\cdot10^{-5}$ mol L^{-1}, and those on methyl oleate oxidation were carried out at $W_i = 1\cdot10^{-7}$ mol L^{-1} s^{-1} and [ArOH] = $(2.0—4.0)\cdot10^{-4}$ mol L^{-1}.

The oxidation of lard (produced at the Novosibirsk Meat-Packing Industrial Complex) was performed according to a described[24] procedure using oxygen bubbling at 130 °C. The weight of the oxidized sample was 50 g, and the concentration of the inhibitors was 1.5 mmol g^{-1}. During experiment 1-g samples were taken, and the concentration of the peroxide compounds were determined by the iodometric method.[25] The time, during which lard was oxidized to the peroxide number 0.1, was used as the induction period.

Hexadecane was oxidized at 180 °C in a gasometric setup similar to that described earlier[15] at an oxygen pressure of 1 atm. The total volume of the sample was 5 mL and [ArOH] = 8.0 mmol L^{-1}. The kinetic curves were plotted on the basis of the obtained data. Using these kinetic curves, the induction period was determined as the intersection point of two tangents to the kinetic curve corresponding to the initial and final rates of hexadecane oxidation.

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