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Reaction of Sterically Congested Phenols and Quinones with Organic Radicals

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Abstract — In the course of radiation-induced free-radical transformations of hexane and ethanol, pyrocatechol and hydroquinone derivatives, as well as their respective quinones, are more effective than phenol and resorcinol derivatives in controlling reactions that involve alkyl and hydroxyalkyl radicals. The opposite result takes place in the inhibition by phenols of hexane oxidation in which the key role belongs to the peroxyl radicals generated from the starting compounds.

Phenol, di- and polyphenol derivatives are widely known industrial [1] and natural [2] antioxidants, which brings interest in their properties. Considerable attention has been given to correlations between the structure of phenolic compounds and their antioxidant activity. It is commonly accepted that the ability of phenols to inhibit oxidation of organic compounds is determined by their high reactivity toward peroxyl ($ROO^{\cdot}$) and other oxygen-centered radicals [1, 2].

The main concept we develop in our studies is that processes involving $ROO^{\cdot}$ and other reactive oxygen species are not the only ones responsible for damage of biosystems and industrial materials. Specifically, it was shown that fragmentation of carbon-centered radicals can cause destruction and modification of lipids [3, 4], peptides [5], carbohydrates [6], and other biologically important molecules. Peroxide oxidation of synthetic and natural objects, too, begins with generation of carbon-centered radicals from the starting materials. Reactions of carbon-centered radicals with phenolic compounds have scarcely been studied [1, 7]. In this connection we have performed a comparative assessment of the reactivity of phenol, di-, and polyphenol derivatives toward oxygen- and carbon-centered radicals [8, 9].

In the present work we studied the effect of sterically congested phenolic compounds on radiochemical transformations of hexane and ethanol. The resulting data allow us to judge about the reactivity of the compounds studied toward oxygen- and carbon-centered organic radicals.

It is known that radiolysis of hexane involve reactions leading to hexyl radicals [10] whose recombination gives dodecanes [schemes (1)–(6)].

$$C_6H_{14} \rightsquigarrow C_6H_{14}^{\cdot+}, \bar{e}, C_6H_{14}^{**}, \quad (1)$$

$$C_6H_{14}^{\cdot+} + \bar{e} \longrightarrow C_6H_{14}^{**}, \quad (2)$$

$$C_6H_{14}^{**} \longrightarrow H_2 + C_6H_{12}, \quad (3)$$

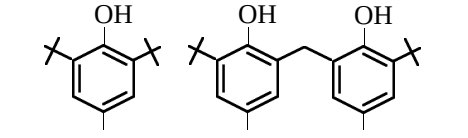
$$C_6H_{14}^{**} \longrightarrow H + \dot{C}_6H_{13},$$

$$H^{\cdot} + C_6H_{14} \longrightarrow \dot{C}_6H_{13} + H_2, \quad (4)$$

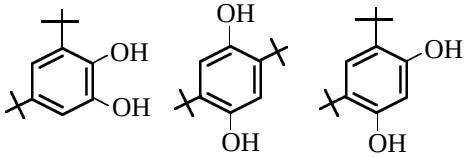
$$2\dot{C}_6H_{13} \longrightarrow C_6H_{14} + C_6H_{12}, \quad (5)$$

$$2\dot{C}_6H_{13} \longrightarrow C_{12}H_{26}. \quad (6)$$

Consequently, by measuring the total yield of dodecanes in the presence of additives, one can assess the reactivity of the latter toward alkyl radicals. From the plots of the accumulation of final products of hexane radiolysis vs. absorbed dose (see figure) we calculated the total yields of dodecanes G(R–R) (see table) formed by the recombination of hexyl radicals with an unpaired electron on C^2 or C^3. From the resulting data it follows that sterically congested diphenols **III** and **IV** [except for 4,6-di-*tert*-butylresorcinol (**V**)] and quinones **VI** and **VII** more effectively react with alkyl radicals than phenol derivatives, such as industrial antioxidants Ionol (**I**) and Agidol (**II**).



I **II**



III **IV** **V**

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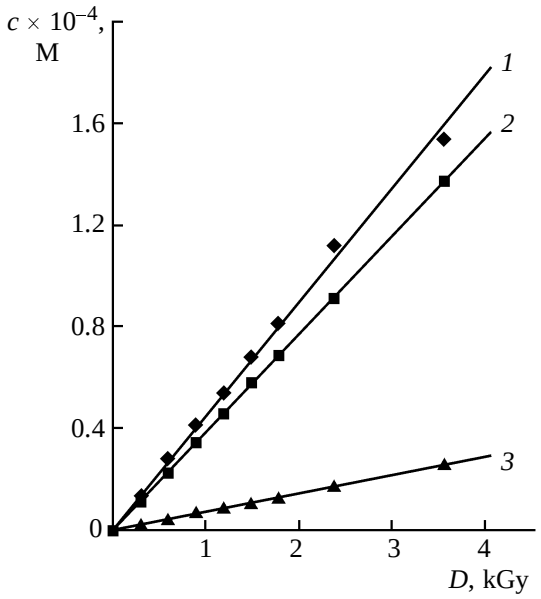
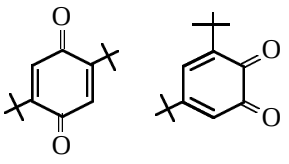


Plots of the total concentration (*c*) of dodecanes (formed by recombination of hexyl radicals with the unpaired electrons on C^2 and C^3) on absorbed dose (*D*) in deaerated hexane (*1*) without additives and in the presence of 10^{-3} mol l^{-1} of (*2*) Ionol (**I**) and (*3*) di-*tert*-butylpyrocatechol (**III**).



VI **VII**

Effect of sterically congested phenols and quinones ($c \times 10^{-3}$ M) on the radiochemical yields ($G \times 10^7$, J mol^{-1}) of the products of radiolysis of hexane and ethanol

Comp. no.	Hexane + Ar, ΣG(R–R)	Hexane + O_2, ΣG(OX)	Ethanol + Ar	
			CH_3CHO	2,3-butanediol
–	0.44 ± 0.01	1.53 ± 0.08	1.61 ± 0.10	1.38 ± 0.02
I	0.37 ± 0.02	0.66 ± 0.03	1.31 ± 0.07	1.10 ± 0.04
II	0.20 ± 0.01	0.70 ± 0.04	–	–
III	0.060 ± 0.003	1.10 ± 0.06	2.30 ± 0.10	0.60 ± 0.08
IV	0.070 ± 0.003	1.21 ± 0.07	2.35 ± 0.20	0.42 ± 0.06
V	0.140 ± 0.007	0.42 ± 0.02	1.15 ± 0.08	1.25 ± 0.02
VI	0.050 ± 0.005	1.60 ± 0.018	3.14 ± 0.32	0.060 ± 0.003
VII	0.050 ± 0.005	1.52 ± 0.08	–	–

In the presence of oxygen, radiolysis of hexane is accompanied by oxidation of the starting compound. Hexanols and hexanones are major stable molecular products formed by scheme (7).

$$R^{\cdot} + O_2 \longrightarrow ROO^{\cdot} \rightarrow\rightarrow\rightarrow \text{2-hexanol, 3-hexanol, 2-hexanone, 3-hexanone.} \quad (7)$$

The total radiochemical yields of the products [ΣG(OX)] formed by scheme (7) in the presence of atmospheric oxygen suggest that phenols **I**, **II**, and **V** surpass diphenols **III** and **IV** in their ability to inhibit oxidation of hydrocarbons.

As already noted, the key reaction in the inhibition of oxidation of organic compounds with phenols is reaction of the latter with the $ROO^{\cdot}$ radicals [scheme (8)].

$$ROO^{\cdot} + PhOH \longrightarrow ROOH + PhO^{\cdot}. \quad (8)$$

The rate constant of reaction (8) with Ionol (**I**) is lower than those for compounds **III** and **IV** by about two orders ofmagnitude [1, 11–13], and, at the same time, as judged from the yields of the final products, phenols **I** and **II** suppress hexane oxidation more effectively than diphenols **III** and **IV** (Table 1). The same effect has been noted by Burlakova *et al*. [14] in their study on the antioxidant activity of Ionol (**I**) and α-tocopherol. This phenomenon has not yet got a satisfactory explanation and, in our view, deserves special investigation

Processes that take place on γ irradiation of ethanol have been studied in detail [15]. It was shown that the major radiolysis products are 2,3-butanediol and acetaldehyde, that are formed by biradical reactions of the α-hydroxyethyl radical [schemes (9) and (10)].

$$2CH_3\dot{C}HOH \longrightarrow CH_3CH(OH)CH(OH)CH_3, \quad (9)$$

$$2CH_3\dot{C}HOH \longrightarrow CH_3CHO + C_2H_5OH. \quad (10)$$

Our results show that phenol or quinone additives may substantially affect the ratio of the yields of the products formed by reactions (9) and (10). Specifically, diphenols and quinones suppress formation of 2,3-butanediol, and the yield of acetaldehyde in this case increases. As to Ionol (**I**) and compound **V**, their presence in ethanol slightly decreases that yields of both 2,3-butanediol and acetaldehyde. This result means that compounds **III**, **IV**, **VI**, **VII** and **I**, **IV** react with α-hydroxyalkyl radicals by different mechanisms. It is known that compounds **III** and **IV** can form in homolytic reactions quinoid structures that can oxidize alcohol radicals by reaction (11) [8, 16].

$$R\dot{C}HOH + {}^{\cdot}OH(Q) \longrightarrow RCHO + QH_2({}^{\cdot}OH). \quad (11)$$

Here ${}^{\cdot}OH$ are semiquinone radicals, and Q are quinones.

Reaction (11) underlies the suppression by compounds **III, IV, VI** of 2,3-butanediol formation and the increase of the yield of acetaldehyde in ethanol radiolysis. Compounds **I** and **IV** under the same conditions are unable to form quinones and react instead with the $CH_3\dot{C}HOH$ radicals, thus decreasing the yields of 2,3-butanediol and acetaldehyde.

Thus, on the strength of the above results we can draw the following conclusion: Phenolic and quinoid compounds can not only inhibit oxidation, but also effectively control various reactions of carbon-centered radicals. This property is intrinsic in diphenol derivatives that are capable of forming quinoid structures in the course of homolytic transformations and explains the higher reactivity of such derivatives toward carbon-centered radicals.

EXPERIMENTAL

The ^{1}H NMR spectra of compounds in $CDCl_3$ were obtained on a JNM PS-100 instrument against HMDS. The mass spectra were recorded on a Shimadzu QP-500 spectrometer at 70 eV with direct sample admission into the ion source.

2,6-Di-*tert*-butyl-4-methylphenol (**I**) and 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) (**II**) (Aldrich) were purified by vacuum sublimation or crystallization from hexane; hexane (Baker Analyzed, 99%) was used as received.

3,5-Di-*tert*-butylpyrocatechol (**III**) [17], 2,5-di-*tert*-butylhydroquinone (**IV**) [18], and 4,6-di-*tert*-butylresorcinol (**V**) were obtained by alkylation of pyrocatechol, hydroquinone, and resorcinol, respectively, with *tert*-butyl alcohol in the presence of sulfuric acid.

4,6-Di-*tert*-butylresorcinol (V). To a solution of 5.5 g of resorcinol and 9 g of *tert*-butyl alcohol in 20 ml of glacial acetic acid, 6 ml of 98% sulfuric acid was added dropwise at 20–25°C with stirring. After 1 h, the reaction mixture was poured into 200 ml of water, the precipitate that formed was filtered off, washed with water, and dried in air. Recrystallization from hexane gave 7.5 g (67%) of compound **V** as a colorless powder, mp 69–70°C. ^{1}H NMR spectrum, δ, ppm: 7.11 s, (5H, 5CH), 6.07 s (2H, 2CH), 5.0–4.7 (1H, OH), 1.36 s (9H, $3CH_3$), 1.32 s (9H, $3CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 222, (12) $[M]^+$, 207 (100) $[M - CH_3]$.

2,5-Di-*tert*-butyl-1,4-benzoquinone (**VI**) and 3,5-di-*tert*-butyl-1,2-benzoquinone (**VII**) were obtained by oxidation of the corresponding diphenols [19].

Initiation of the free radical transformations in the model systems was performed by expose of them to γ-irradiation (^{137}Cs). Deaerated solutions were prepared by bubbling high-purity (99.9%) argon for 1.5 h through a chosen solvent (hexane or ethanol), and then weighed portions of the compounds to be studied were dissolved in thus prepared solvent under argon. The solutions were placed into glass ampoules, sealed, and subjected to ^{137}Cs irradiation. The absorbed dose rates were 0.32 to 0.01 Gy sec^{-1}, the used doses were within the range 0.2–4 kGy.

Analysis of hexane irradiation products (isomeric dodecanes) was performed by GLC on a a Shimadzu GC-17 AAF/APC chromatograph using a DB-5 quartz capillary column (30.000 × 0.54 mm), initial temperature 100°C, programmed first at 8 deg min^{-1} to 200°C and then at 10 deg min^{-1} to 270°C; flame ionization detector, detector temperature 220°C, injector temperature 250°C, carrier gas nitrogen (3.7 ml min^{-1}).

Analysis of hexane free-radical oxidation products (2- and 3-hexanols) was performed under the same conditions except for the temperature program (initial temperature 60°C, programmed at 8 deg min^{-1} to 180°C and then maintained at that temperature for 2 min) and rate of carrier gas (1.8 ml min^{-1}).

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REFERENCES

1. Roginskii, V.A., *Fenol'nye antioksidanty. Reaktsionnaya sposobnost' i effectivnost'* (Phenolic Antioxidants. Reactivity and Effectivity), Moscow: Nauka, 1988, p. 248.
2. Hallwell, B. and Gutteridge, J.M.C., *Free Radicals in Biology and Medicine*, Oxford: Clarendon, 1999, p. 937.
3. Muller, S.N., Batra, R., Senn, M., Giese, B., Kisel, M., and Shadyro, O., *J. Am. Chem. Soc.*, 1997, vol. 119, no. 12, p. 2759.
4. Shadyro, O.I., Yurkova, I.I., and Kisel, M.A., *Int. J. Rad. Biol.*, 2002, vol. 78., no. 3, p. 211.
5. Shadyro, O.I., Sosnovskaya, A.A., and Vrublevskaya, O.N., *Int. J. Rad. Biol.*, 2003, vol.79, no. 4, p. 269.
6. Shadyro, O.I., in: *NATO ASI*, Ser. 3, *High Technology*, Minisci, F., Ed., Dobrecht: Kluwer., 1997, vol. 27, p. 317.

7. Franchi, P., Lucarini, M., Peduli, G.F., Valgimigli, L., and Lunelli, B., *J. Am. Chem. Soc.*, 1999, vol. 121, no. 3, p. 507.
8. Shadyro, O.I., Glushonok, G.K., Glushonok, T.G., Edimicheva, I.P., Moroz, A.G., Sosnovskaya, A.A., Yurkova, I.L., and Polozov, G.I., *Free Rad. Res.*, 2002, vol. 36, no. 8 , p. 859.
9. Shadyro, O.I., Edimecheva, I.P., Glushonok, G.K., Ostrovskaya, N.I., Polozov, G.I., Murase, H., and Kagiya, T., *Free Rad. Res.*, 2003, vol. 37, no. 19, p. 1087.
10. Gäumann, T. and Hoigne, I., *Aspects of Hydrocarbon Radiolysis*, Amsterdam: Elsevier, 1968, p. 213.
11. Burton, G.W., Doba, T., Gabe, E.J., Hughes, L., Lee, F.L., Prasad, L., and Ingold, K.U., *J. Am. Chem. Soc.*, 1985, vol. 107, no. 24, p. 7053.
12. Barclay, L.R., Vinqvist, M.R., Mukai, K., Iton, S., and Morimoto, H., *J. Org. Chem.*, 1993, vol. 58, no. 26, p. 7416.
13. Azatyan, N.A., Karpukhina, G.V., Belostotskaya, I.S., and Komissarova, N.A., *Neftekhimiya*, 1973, vol. 13, no. 3, p. 435.
14. Burlakova, E.B., Alesenko, A.V., Molochkina, E.V., Pal'mina, N.P., and Khrapova, N.G., *Biooksidanty v luchevom porazhenii i zlokachestvennom roste* (Bio-oxidants in Radiation Disease and Malignant Growth), Moscow: Nauka, 1975, p. 214.
15. Freeman, G.R., *The Study of Fast Processes and Transient Species by Pulse Electron Radolysis*, Dordrecht: Reidel, 1982, p. 399.
16. Simic, M. and Hayon, E., *Biochem. Biophys. Res. Commun.*, 1973, vol. 50, p. 364.
17. Erickson, E.R. and Falls, N., US Patent 2.439.421, *Chem. Abstr.*, 1949, vol. 42, no. 19, p. 7336.
18. Schulze, H. and Flaig, W., *Justus Liebigs Ann. Chem.*, 1952, vol. 573, no. 3, p. 231.
19. Flaig, W., Ploetz, t., and Biergans, H., *Justus Liebigs Ann. Chem.*, 1955, vol. 597, no. 3, p. 196.