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Pyrocatechol and Its Derivatives as Antioxidants and Prooxidants

V. S. Kosobutskii

Belarus State University, pr. Nezavisimosti 4, Minsk, 220030 Belarus
e-mail: kasabutski@bsu.by

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Abstract—The effect of pyrocatechol and its derivatives (4,5-dichloro- and 4,5-dibromo pyrocatechols, veratrol, 4,5-dichloro- and 4,5-dibromoveratrol) on the free-radical oxidation of propan-2-ol in aqueous solutions, initiated by γ-radiation. Pyrocatechol and dihalocatechols exhibit antioxidant properties, whereas dihaloveratrols exhibit prooxidant properties. Dibromoveratrol showed more expressed prooxidant properties.

Keywords: pyrocatechol, veratrol, free-radical oxidation, reaction rate

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Free-radical oxidation involving formation of reactive oxygen species occur in all anaerobic tissues and represents one of the types of normal metabolic processes. The deviation of the free-radical reaction rate from the norm, specifically, when it occurs either faster or slower, may cause free-radical pathology [1, 2]. Free-radical oxidation reactions can be normalized by means of both antioxidants and prooxidants. In the present work we studied the effect of pyrocatechol and its derivatives (4,5-dibromo- and 4,5-dichlorocatechols, veratrol, and 4,5-dibromo- and 4,5-dichloroveratrols) on the free-radical oxidation of propan-2-ol.

The free-radical oxidation of propan-2-ol was initiated by γ-irradiation of oxygen-saturated 5 M aqueous solutions. The concentration of oxygen in the solutions was 0.0022 M, and the concentration of pyrocatechol and its derivatives was 1×10^{-4} M. The low concentrations of the additives were chosen so that they did not react with radical products of water radiolysis. Under irradiation water undergoes radiolysis to form reactive species: OH, $\bar{e}_{aq}$, H_3O^+, H, and H_2O_2 with the radiation chemical yields of 2.7, 2.7, 2.7, 0.55, and 0.7 molecules/100 eV, respectively [3, 4]. Further they react by reactions (1)–(8).

$$H + O_2 \rightarrow HO_2^{\cdot},\ k_1\ 2.1 \times 10^{10}\ L\ mol^{-1}\ s^{-1}\ [5, 6], \quad (1)$$

$$\bar{e}_{aq} + O_2 \rightarrow O_2^{-\cdot},\ k_2\ 1.8 \times 10^{10}\ L\ mol^{-1}\ s^{-1}\ [5, 6], \quad (2)$$

$$(Me)_2CHOH + H \rightarrow (Me)_2\dot{C}OH + H_2,$$

$$k_3\ 8.2 \times 10^7\ L\ mol^{-1}\ s^{-1}\ [4], \quad (3)$$

$$(Me)_2CHOH + {}^{\cdot}OH \rightarrow (Me)_2\dot{C}OH + H_2O,$$

$$k_4\ 2.1 \times 10^9\ L\ mol^{-1}\ s^{-1}\ [4], \quad (4)$$

$$(Me)_2\dot{C}OH + O_2 \rightarrow (Me)_2CO + H^+ + O_2^{-\cdot},$$

$$k_5\ 683\ s^{-1}\ [7, 8], \quad (5)$$

$$O_2^{-\cdot} + O_2^{-\cdot} + 2H_2O \rightarrow H_2O_2 + O_2 + 2HO^-,$$

$$k_6\ 0.15\ L\ mol^{-1}\ s^{-1}\ [7, 9, 10], \quad (6)$$

$$k_7\ 15\ L\ mol^{-1}\ s^{-1}\ [4, 10, 11], \quad (7)$$

$$O_2^{-\cdot} + H_2O_2 \rightarrow HO^- + {}^{\cdot}OH + O_2,$$

$$O_2^{-\cdot} + H^+ \leftrightarrow HO_2^{\cdot},\ pK\ 4.7\ [7]. \quad (8)$$

These reactions form acetone with the radiation chemical yield 6.15 ± 0.36 molecules/100 eV. Figure 1 show the dependence of the accumulation of acetone on radiation dose. When pyrocatechol is added to the solution, the radiation chemical yield of acetone decreases to 4.31 ± 0.39 molecules/100 eV. The decreased yield of acetone is associated with the occurrence of reaction (9).

$$O_2^{-\cdot} + (HO)_2C_6H_4 \rightarrow H_2O_2 + {}^{\cdot}OC_6H_4O^-. \quad (9)$$

The rate constants of these reactions of superoxide ion with 1,4-hydroquinone and 2,5-dichloro-1,4-hydroquinone are 1.6×10^7 L mol^{-1} s^{-1} [4] and 1.3×10^7 L mol^{-1} s^{-1} [12], respectively. Decreased yields of acetone were also observed with 4,5-dichlorocatechol and 4,5-dibromocatechol (c 1×10^{-4} M) additives, but these additives decreased the yield of acetone stronger than pyrocatechol (to 3.92 ± 0.38 and 3.16 ±

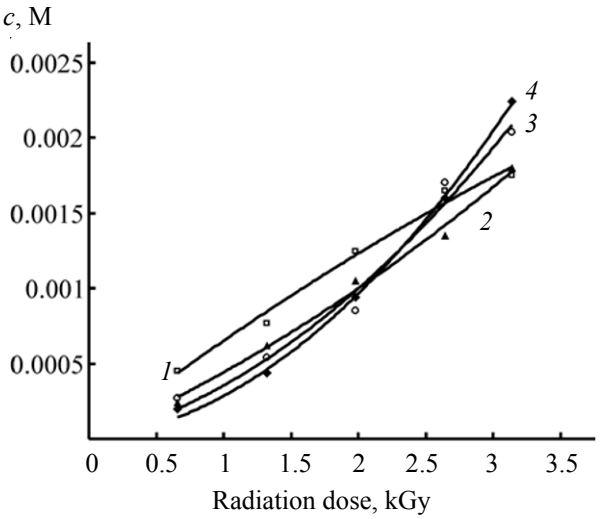

Fig. 1. Dependence of the concentration of acetone on the irradiation dose of a 5 M solution of propan-2-ol (*1*) without additions and in the presence of (*2*) pyrocatechol, (*3*) 4,5-dichloropyrocatechol, and (*4*) 4,5-dibromopyrocatechol. Absorbed dose rate (*P*) 0.55 Gy/s.

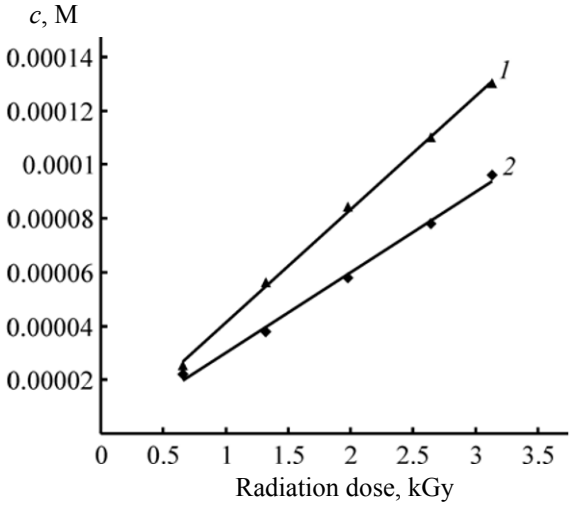

Fig. 2. Dependence of the concentration of (*1*) bromide and (*2*) chloride ions on the irradiation dose of a 5 M solution of propan-2-ol in the presence of 4,5-dibromopyrocatechol and 4,5-dichloropyrocatechol. *P* 0.55 Gy/s.

0.35 molecules/100 eV, respectively). Moreover, dichloro- and dibromocatechol appreciably affected the kinetics of acetone accumulation. The initial portion of the kinetic curve shows an induction period, which implies inhibition of the oxidation reaction. Dihalocatechols can react with superoxide ion by reactions (10) and (11). Reaction (10) is analogous to reaction (9).

$$O_2^{-\cdot} + (HO)_2C_6H_2Hlg_2 \rightarrow H_2O_2 + {}^{\cdot}OC_6H_2Hlg_2O^-, \quad (10)$$

$$O_2^{-\cdot} + (HO)_2C_6H_2Hlg_2 \rightarrow O_2 + (HO)_2\dot{C}_6H_2Hlg + Hlg^-, \quad (11)$$

$$(HO)_2\dot{C}_6H_2Hlg \rightarrow {}^{\cdot}OC_6H_3HlgO^- + H^+. \quad (12)$$

Reaction (12) involves rapid transformation of σ-radical $(HO)_2\dot{C}_6H_2Hlg$ to semiquinone π-radical ${}^{\cdot}OC_6H_2HlgO^-$. The rate constant of a similar isomerization reaction of hydroxyphenyl σ-radical C_6H_4OH into phenoxyl is 1.7×10^5 s^{-1} [13]. Evidence for reaction (11) is provided by the formation of halide ions on the radiolysis of solutions. Similar reactions of superoxide ion with chlorinated aromatic compounds were observed in [14]. Figure 2 shows the dependences of the concentration of halide ions on radiation dose. The radiation chemical yields of bromide and chloride ions were 0.40 ± 0.03 and 0.28 ± 0.03 molecules/100 eV. Dibromocatechol stronger suppress acetone formation and the yield of bromide ions is higher compared to chloride ion. This result is consistent with the relative electron-acceptor capacities of bromoaromatic and chloro-aromatic compounds. Thus, for example, the rate constants of the reactions of C_6H_5Br and C_6H_5Cl with hydrated electron are 4.3×10^9 and 5×10^8 L mol^{-1} s^{-1}, respectively [5, 15].

Halogenation of pyrocatechol enhances its antioxidant properties. Therewith, bromo derivatives are stronger antioxidants than chloro derivatives.

The rate of reaction (2) of $\bar{e}_{aq}$ with O_2 at halocatechol and haloveratrol concentrations of 0.0001 M is ~40 times as high as the reaction rate of hydrated electron with halocatechols and haloveratrols, and the radiation chemical yield of halide ions formed by this reaction should not be higher than 2.7/40 ≈ 0.07 molecules/100 eV. The minimal observed yield of chloride ions $G_{C^-_1}$ is 0.28 ± 0.03 molecules/100 eV. At such a low concentration of additives electrons were virtually completely consumed in the reaction with oxygen. The formation of halide ions at such concentrations is associated with reactions (11) and (13).

Veratrol did not affect the radiation chemical yield of acetone (6.1 ± 0.5 molecules/100 eV). In the presence of dihaloveratrols, the yields of acetone increased to 6.6 ± 0.2 and 6.9 ± 0.3 molecules/100 eV with 4,5-dichloro- and 4,5-dibromoveratrol, respectively. Figure 3 presents the dependences of acetone accumulation in the absence and in the presence of dihaloveratrols. The same figure also shows the dependences of the concentrations of chloride and

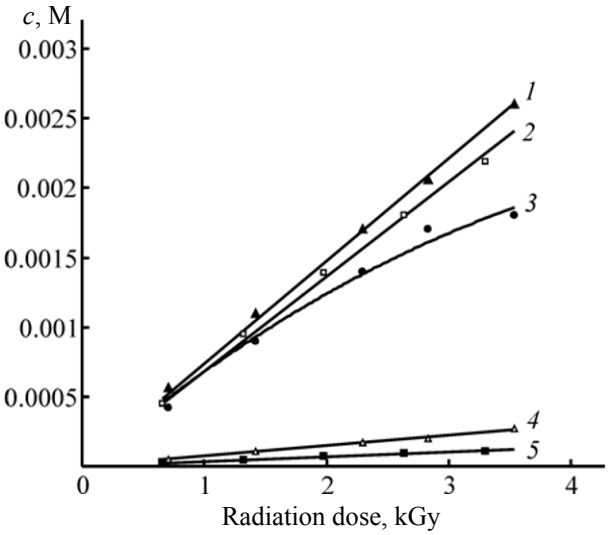

Fig. 3. Accumulation of (*1*–*3*) acetone and (*4*) bromide and (*5*) chloride ions as a function of the irradiation dose of a 5 M solution of propan-2-ol (*3*) without additions and in the presence of (*1*, *4*) 4,5-dibromoveratrol and (*2*, *5*) 4,5-dichloroveratrol. *P* 0.55 Gy/s.

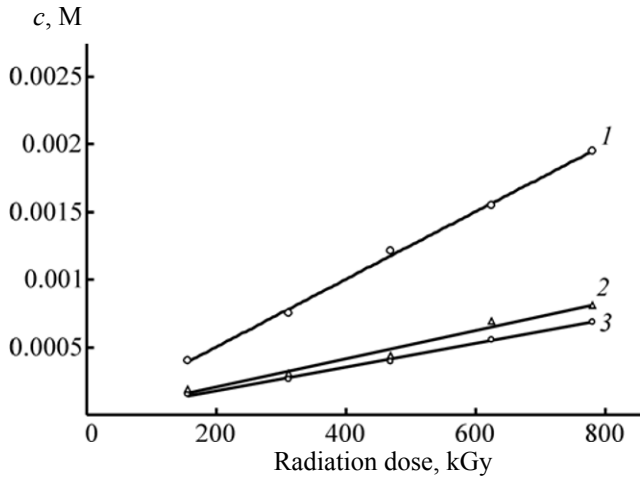

Fig. 4. Dependence of the concentration of acetone on the irradiation dose of a 5 M solution of propan-2-ol (*3*) without additions and in the presence of (*1*) 4,5-dibromoveratrol and (*2*) 4,5-dichloroveratrol. *P* 0.26 Gy/s.

bromide ions on the radiation dose of dihaloveratrol-containing solutions. The radiation chemical yields of halide ions were 0.72 ± 0.04 molecules/100 eV with 4,5-dibromoveratrol and 0.35 ± 0.03 molecules/100 eV with 4,5-dichloroveratrolом. The yield of acetone is increased due to reactions (13) and (14).

$$O_2^{\cdot-} + (MeO)_2C_6H_2Hlg_2 \rightarrow O_2 + (MeO)_2\dot{C}_6H_2Hlg + Hlg^-, \quad (13)$$

$$(MeO)_2\dot{C}_6H_2Hlg + (Me)_2CHOH \rightarrow (Me)_2\dot{C}OH + (MeO)_2C_6H_3Hlg. \quad (14)$$

Reaction (14) occurs rapidly to form the radical $(Me)_2\dot{C}OH$. The rate constant of a similar reaction of σ-radical 4-$HO^-\dot{C}_6H_4$ with propan-2-ol is (1–3) × 10^7 L mol^{-1} s^{-1} [14]. The fact that the yield of acetone increases in the presence of dihaloveratrols points to prooxidant properties of the latter. The prooxidant activity of dihaloveratrols is enhanced with increasing concentration of dihaloveratrols and decreasing absorbed dose rate. Thus, in analogous oxygen-saturated propan-2-ol solutions at dichloroveratrol and dibromoveratrol concentrations of 1 × 10^{-3} M and dose rate 0.26 Gy/s, the yield of acetone increases to 10.1 ± 0.8 and 22 ± 2 molecules//100 eV, respectively. At the same time, in the absence of dihaloveratrols, the yield of acetone in 5 M propan-2-ol saturated with oxygen at the dose rate 0.26 Gy/s was 8.4 ± 0.7 molecules/100 eV. Figure 4 demonstrates the effect of dihaloveratrols under the same conditions. As the dose rate was decreased ~2 times, the steady-state concentration of superoxide ions and their disproportionation rate [reaction (6)] decreased. In its turn, the rate of reaction (7) increased, and the yield of acetone in the absence of dihaloveratrols increased from 6.15 to 8.4 molecules/100 eV. In the presence of dihaloveratrols in the concentration higher by an order of magnitude (1 × 10^{-3} M), reaction (13) of $O_2^{\cdot-}$ with dihaloveratrols strongly accelerated, which led to a considerable increase of the yield of acetone in the oxidation of propan-2-ol with oxygen in the presence of dihaloveratrols. It should be noted that dibromoveratrol is a stronger prooxidant than dichloroveratrol. This fact is explained by a higher electron-acceptor power of brominated aromatic compounds compared to the respective chlorinated compounds.

Thus, bromine and chlorine substitution in pyrocatechol enhances its antioxidant properties. Catechol methyl ethers show no antioxidant activity. Halogenation of 1,2-dimethoxybenzene converts the latter into a pro-oxidant. Bromo derivatives exhibit a more expressed anti- and prooxidant activity than chloro derivatives.

EXPERIMENTAL

Solutions were prepared using twice distilled water and chemical grade propan-2-ol. Saturation with oxygen was performed in a syringe; as this took place, air in the solutions was replaced by oxygen. 1,2-

Dihydroxybenzene, 1,2-dimethoxybenzene, 4,5-dichloro-1,2-dihydroxybenzene, and 4,5-dibromobenzene-1,2-dihydroxybenzene were purchased from Sigma–Aldrich. 4,5-Dibromo-1,2-dimethoxybenzene was synthesized by the bromination of 1,2-dimethoxybenzene in carbon tetrachloride by the known procedure [16]. 4,5-Dichloro-1,2-dimethoxybenzene was prepared by the chlorination of veratrol with benzyltrimethylammonium tetrachloroiodate in acetic acid by the procedure in [17]. Irradiation of the solutions (Co^{60} γ-radiation) was performed in sealed ampules. The absorbed radiation dose was measured using a ferric sulfate dosimeter. Analysis of halide ions was performed by potentiometric titration with silver nitrate. Acetone was analyzed by GLC with flame ionization detector, carrier gas hydrogen. The radiation chemical yields of acetone and halide ions were calculated from the dependences of their concentrations from radiation dose. The concentrations of oxygen were determined by gas adsorption chromatography with a thermal conductivity detector, carrier gas helium.

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