

Electron Transfer from Quinone and Nitroarene Anion Radicals to Molecular Oxygen Studied by the Potential-step Chronocoulometry Method

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Catalytic activity of quinones and nitroarenes, as mediators in the reductive activation of molecular oxygen, can be evaluated by using potential-step chronocoulometry.

Reaction of active oxygen species with biomolecules is thought to be responsible for oxidative cytotoxicity. One of the most critical reactions *in vivo* for the generation of active oxygen species is the formation of superoxide anion radical ($O_2^{\cdot-}$) by one-electron reduction of molecular oxygen (O_2).¹ Other active oxygen species, such as hydroxyl radical, hydroperoxide, *etc.*, are formed *via* $O_2^{\cdot-}$. Well known one-electron reductants of O_2 are anion radicals. Semiquinone anion radicals ($SQ^{\cdot-}$) are readily oxidized to quinones under aerobic conditions accompanied by the formation of $O_2^{\cdot-}$.² The $O_2^{\cdot-}$ is also generated by the interaction of nitroarene anion radicals ($NA^{\cdot-}$) and O_2 .³ Further reduction of $NA^{\cdot-}$ by nitroreductase to mutagenic and carcinogenic nitroso and then hydroxylamino derivatives is thus inhibited by O_2 .⁴ We have already clarified that the reaction of anion radicals with O_2 is directly detectable by the potential-step chronocoulometry (PSCC) technique.⁵ The purpose of the present investigation is to establish a chemical basis the ability of formation of $O_2^{\cdot-}$ by $SQ^{\cdot-}$ and $NA^{\cdot-}$.

Electron transfer from anthraquinone (AQ) anion radical to O_2 was monitored by cyclic voltammetry (CV). As can be seen in Fig. 1, the CV of dimethylformamide (DMF) saturated with O_2 showed cathodic (-1427 mV *vs.* Ag/Ag^+) and anodic (-1038 mV *vs.* Ag/Ag^+) peaks corresponding to the reduction of O_2 and oxidation of $O_2^{\cdot-}$, respectively. When 0.1 mmol dm^{-3} of AQ was added to the O_2 -saturated DMF solution, a reduction peak (E_{pc}) at -1333 mV was detected. The positive shift of E_{pc} from -1427 mV to -1333 mV upon addition of AQ can be explained as follows: as the E_{pc} of AQ is higher than that of O_2 , AQ is more reducible than O_2 under these electrochemical conditions. Initially, AQ is electrochemically reduced at the cathode to an anion radical which then transfers one electron to O_2 to generate $O_2^{\cdot-}$ and reforms AQ. Regenerated AQ is then again electrochemically reduced to an anion radical. Since, under these conditions, the concentration of O_2 is significantly higher than that of AQ, AQ is turned over and consumes the excess O_2 . As a result, the catalytic amount of AQ acts as a mediator for the

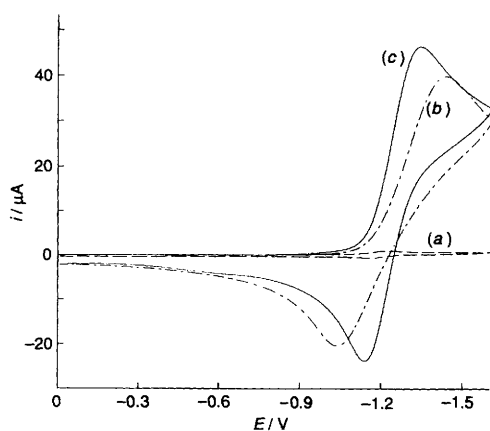


Fig. 1 CV of 0.1 mmol dm^{-3} anthraquinone under argon (a), saturated O_2 (b) or anthraquinone under saturated O_2 (c) in DMF solutions (1 ml) containing 0.1 mol dm^{-3} NEt_4ClO_4 at a Pt electrode (diameter 1.6 mm) with a scan rate of 100 mV s^{-1} at 25 °C. The potentials are *vs.* Ag/Ag^+ (0.01 mol dm^{-3} $AgNO_3$ in 0.1 mol dm^{-3} NBu_4ClO_4 in MeCN).

generation of $O_2^{\cdot-}$. The most aspect for the catalytic action of AQ is that AQ has a more positive E_{pc} than O_2 .

To evaluate the electron transfer ability of quinones and nitroarenes, the PSCC technique was employed.⁶ In the PSCC experiment, the cathodic potential was stepped from an initial value (0 mV) where no redox reaction occurred to a final value (E_{pc} of substrate) where one-electron reduction of substrate occurred and then the integration of current was measured for 250 ms. Turnover numbers of quinones and nitroarenes were calculated from the slope of the Anson plot (charge- $t^{1/2}$ plot). Fig. 2 shows typical results for AQ. The potential was stepped from 0 to -1216 mV (the E_{pc} of AQ, *vs.* Ag/Ag^+). Curve (a) shows the charge-time response when AQ (0.1 mmol dm^{-3}) was reduced in the absence of O_2 . When AQ was reduced in O_2 -saturated DMF, a larger current flowed and the charge-time response curve (c) was obtained. The response curve (b) was obtained for an O_2 -saturated DMF solution in the absence of AQ. Increased charge-time response in curve (c) compared with curves (b) and (a) corresponds to the catalytic action of AQ in the one-electron reduction of O_2 . The amount of $O_2^{\cdot-}$

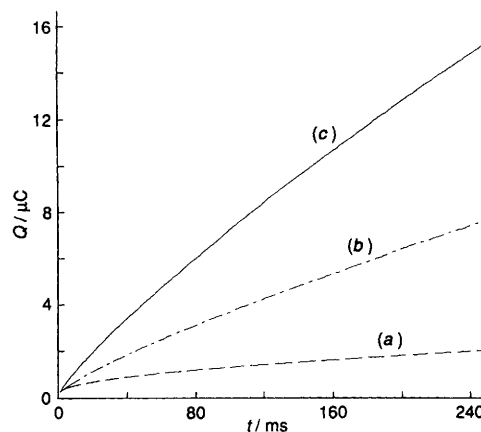


Fig. 2 Chronocoulometry of 0.1 mmol dm^{-3} anthraquinone under argon (a), saturated O_2 (b) or anthraquinone under saturated O_2 (c). The potentials are stepped from 0 to -1216 mV (E_{pc} of anthraquinone) for 250 ms. Other conditions are as in Fig. 1.

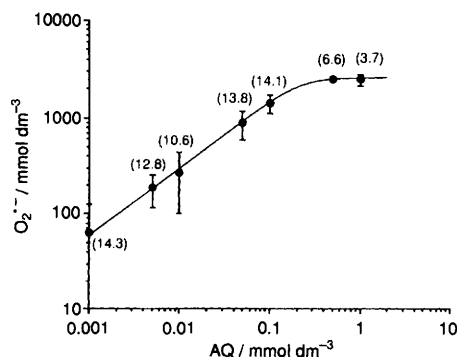


Fig. 3 Effect of anthraquinone concentration on the catalysing formation of $O_2^{\cdot-}$. Each point represents the mean value of three runs, and the error bars indicate the standard deviation. Turnover numbers are given in parentheses for each concentration.

Table 1 Chronocoulometric data of quinones and nitroarenes in the presence or absence of oxygen

Compounds	$E_{pc}1^a$ (mV vs. Ag/Ag ⁺)	[S] ^b / $\mu\text{C ms}^{-1}$	[S + O ₂] ^b / $\mu\text{C ms}^{-1}$	[O ₂] ^b / $\mu\text{C ms}^{-1}$	O ₂ ^{-c} /mmol dm ⁻³	Turnover number ^d
Quinone						
Benzoquinone	-812	0.022	0.027	0.006	1	0
1,4-Naphthoquinone	-981	0.019	0.037	0.017	3	0
1-Hydroxyanthraquinone	-1052	0.018	0.048	0.030	9	0.1
Menadione	-1071	0.018	0.060	0.035	46	0.5
1-Chloroanthraquinone	-1166	0.020	0.389	0.225	786	7.3
Anthraquinone	-1216	0.018	0.755	0.480	1400	14.1
5,12-Naphthacenequinone	-1319	0.019	1.667	1.087	3060	29.7
Nitroarene						
4-Nitroquinoline <i>N</i> -oxide	-1012	0.017	0.041	0.015	43	0.5
1,3-Dinitronaphthalene	-1095	0.018	0.079	0.048	70	0.7
1,7-Dinitronaphthalene	-1134	0.019	0.198	0.107	395	3.9
3-Nitrofluoranthene	-1204	0.019	0.521	0.378	675	6.5
<i>m</i> -Dinitrobenzene	-1227	0.018	0.560	0.400	773	7.8
1,6-Dinitronaphthalene	-1248	0.019	0.738	0.550	928	9.2
1-Nitropyrene	-1325	0.018	1.394	1.086	1580	16.2

^a Applied potential for PSCC experiment. ^b The potentials were stepped from 0 mV to the value E_{pc} for the compounds. Integrations of current were measured for 250 ms with 0.1 mmol dm⁻³ substrate [S] under argon, 0.1 mmol dm⁻³ substrate under saturated O₂ [S + O₂] or saturated O₂ [O₂] in DMF (1 cm³) containing 0.1 mmol dm⁻³ NEt₄ClO₄ at a Pt electrode (diameter 1.6 mm), and the diffusional slopes of a linear plot (charge vs. $t^{1/2}$; Anson plot) were obtained. All values were subtracted by [DMF] as background. The concentration and diffusion coefficient of saturated O₂ in DMF are 4.5 mmol dm⁻³ and 4.7×10^{-5} cm² s⁻¹, reported by J. M. Achord and C. L. Hussey.¹⁰ ^c Amount of generated superoxide = $5450\{[S + O] - ([S] + [O])\}$. ^d Turnover number of redox cycling = $\{[S + O] - ([S] + [O])\}/[S]$.

generated and the AQ turnover number, calculated by the equations in Table 1, is 1400 mmol and 14.1 respectively. Generation of O₂⁻ was examined over a wide range of concentrations of AQ. As shown in Fig. 3, the amount of O₂⁻ generated increased linearly with concentration of AQ within the range 0.001–0.1 mmol dm⁻³ when dissolved O₂ exceeded the concentration of AQ. A plateau was reached at 0.5 mmol dm⁻³ when O₂ was no longer in excess of AQ. The AQ turnover number was almost constant in contrast to the drastic change in the amount of O₂⁻ generated. Similar results were observed when 5,12-naphthacenequinone (5,12-NQ) and 1-nitropyrene (1-NP) were used as mediators. Various quinones and nitroarenes with more positive redox potentials than O₂ were examined by the PSCC method. The number of resultant redox cycles and the amount of production of O₂⁻ are summarized in Table 1. Electron transfer from the anion radicals to O₂ proceeds efficiently by nitroarenes and quinones with a reduction potential (E_{pc}) between -1100 and -1350 mV, and the amount of O₂⁻ generated tends to be increased by a substrate with an E_{pc} close to that of O₂. In particular, AQ, 5,12-NQ and 1-NP are effective mediators for superoxide generation and have redox cycling numbers >14. While the turnover number of AQ is 14.1, those of *m*-dinitrobenzene and 3-nitrofluoranthene, which form their anion radicals at approximately the same E_{pc} as AQ, are 7.83 and 6.50 respectively. These results show that quinone is more responsive as a mediator compared with nitroarenes. No or only weak interaction between anion radicals and O₂ is observed when the substrate E_{pc} is more positive than -1100 mV.

Activation of O₂ by quinone redox cycling has been discussed in connection with quinone E_{pc} values.⁵ There are two independent factors for the generation of O₂⁻ by redox cycling. One is the ease of quinone reduction to form autoxidizable anion radicals for redox cycling.⁶ In reported experiments, quinones with higher E_{pc} values are generally more effective in generating O₂⁻ because they are easier to reduce. Consequently, when the reduction rate is the critical factor for O₂ activation, quinones that have a higher E_{pc} tend to be more effective for generating O₂⁻. An additional factor is the ease of one-electron transfer from anion radicals to O₂. This is an equilibrium reaction and the rate constants become more important for evaluating the O₂⁻ generating ability of

anion radicals. While several reports have discussed the former phenomenon, there are only a few papers that have examined the latter equilibrium. Rao and Hayson⁹ have used pulse radiolysis and kinetic absorption spectrophotometry to determine the rate constants for the reaction of SQ⁻ with O₂ and concluded that the efficiency of electron transfer from anion radicals (electron donors) to O₂ is dependent on the E_{pc} of donor molecules and that quinones with lower E_{pc} values are more effective for O₂ activation. As a result, quinones with higher or lower E_{pc} values have a converse effect on O₂ activation by redox cycling. Our results, which show that SQ⁻ and NA⁻ with lower E_{pc} values are better redox cyclers for O₂ activation, are in accord with the reported results.⁹ Since formation of SQ⁻ and NA⁻ under PSCC conditions is fully supported by electrochemical reduction at the cathode, reaction rates of anion radicals with O₂ can be obtained from both the turnover numbers and the amount of O₂⁻ generated. Thus, the present PSCC method is convenient and useful for evaluating the ability of anion radicals as mediators of reductive O₂ activation and may be useful in the study of other one-electron transfer reactions, whereby its application will be limited to equilibrium reactions. The potential relevance of toxicity caused by redox cycling could be solved by using these results.

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