Kinetics and Mechanism of the Oxidation of 3,5-Di-t-butyl-*o*-benzoquinone with Hydrogen Peroxide in Aqueous Methanol Solution

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The kinetics of the reaction between 3,5-di-t-butyl-*o*-benzoquinone (DTBQ) (1) and hydrogen peroxide have been investigated in 50% aqueous methanol in the pH range 8—10 and an ionic strength of 0.1M using spectrophotometric techniques at temperatures between 19.5 and 36.2 °C. The rate law $-d\,[DTBQ]/dt = k[DTBQ][O_2H^-]$, with k (25 °C) 22.0 ± 0.9 $dm^3\,mol^{-1}\,s^{-1}$ describes the kinetic data. The activation parameters at 25 °C are $\Delta H^\ddagger$ 76 ± 4 kJ mol^{-1} and $\Delta S^\ddagger$ 34 ± 1 J $K^{-1}\,mol^{-1}$. The reaction is subject to specific base catalysis and the rate-determining step is presumably the nucleophilic attack of O_2H^- on the C(1) carbonyl group of DTBQ. The hydroperoxide intermediate so formed breaks down in two ways: (i) to 3,5-di-t-butylmuconic acid anhydride (4), which was detected by g.l.c.–m.s., and (ii) to 6-hydroxy-3,5-di-t-butyl-*o*-benzoquinone (8) which in the reaction with further hydrogen peroxide leads to 5-hydroxy-3,5-di-t-butylmuconic acid anhydride (9). All the products formed in the reaction and identified by g.l.c.–m.s. can be derived from the muconic acid anhydride derivatives (4) and (9).

OXIDATIVE cleavage of catechol is one of the most important reactions catalysed by dioxygenases.[1-4] Catechol is oxidized to *cis,cis*-muconic acid by pyrocatechase[3] and to α-hydroxymuconic semialdehyde by metapyrocatechase.[4]

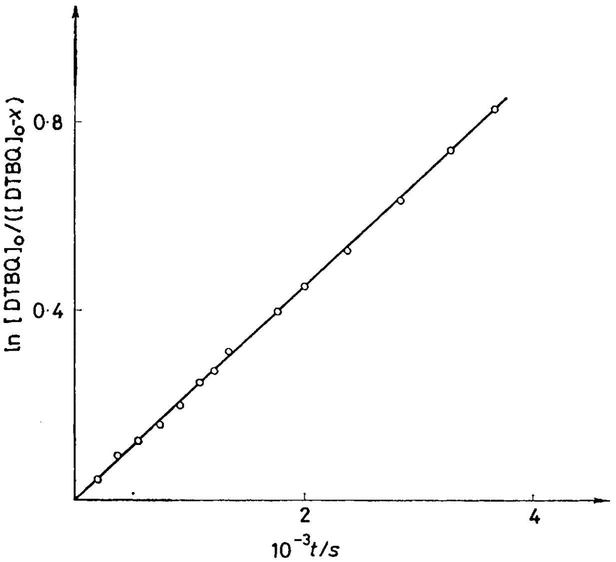


FIGURE 1 log [DTBQ] *versus* time for a typical experiment: [DTBQ] 1.94 × 10^{-3}M; [H_2O_2] 6.94 × 10^{-2}M; pH 9.08; *I* 0.1M; 25 °C

A great number of papers on the biochemical relevance of the ring cleavage reaction are concerned with different model reactions. In some, metal complexes were used as oxidants[5] or catalysts,[6-9] and in others, the autoxidation,[10,11] photo-oxidation,[12] and oxidation of catechols and *o*-quinones with H_2O_2,[13] O_2^-,[14] and per-acids[15,16] have been studied.

Martell *et al.* investigated the kinetics of the autoxidation of 3,5-di-t-butylcatechol in alkaline solution[17] and in the presence of manganese[18] leading exclusively to 3,5-di-t-butyl-*o*-benzoquinone (DTBQ). As a continuation of this work, it was of interest to investigate the kinetics of the subsequent reaction of DTBQ with hydrogen peroxide, since to our knowledge, no kinetic investigation was carried out on the reaction of *o*-quinones with hydrogen peroxide until now. However, a kinetic treatment of the reaction of 1,2-diketones with hydrogen peroxide has been established by Leffler[19] and Bunton *et al.*,[20] respectively.

RESULTS AND DISCUSSION

Upon carrying out the kinetic experiments under pseudo-first-order conditions (with at least a 10-fold excess of hydrogen peroxide) at constant pH and ionic strength, plots of ln $[DTBQ]_0/([DTBQ]_0 - x)$ against time showed good linearity up to 95% conversion (Figure 1). In Figure 2 the initial reaction rates with respect to DTBQ are plotted against initial DTBQ concentration at constant H_2O_2 concentration, pH 9.08, and 0.1M ionic strength. The good linearity of the plots in Figures 1 and 2 indicates that the reaction is first order with respect to DTBQ.

To establish the reaction order in hydrogen peroxide several runs were made under pseudo-first-order conditions at different initial concentrations of hydrogen

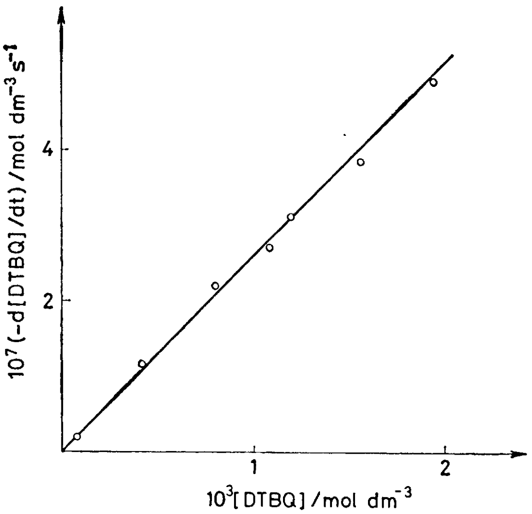


FIGURE 2 Initial reaction rates *versus* initial [DTBQ]: [H_2O_2] 6.94 × 10^{-2}M; pH 9.08; *I* 0.1M; 25 °C

peroxide. On plotting the initial reaction rates as a function of the starting hydrogen peroxide concentration a straight line was obtained (Figure 3) in accord with a first-order dependence on $[H_2O_2]$.

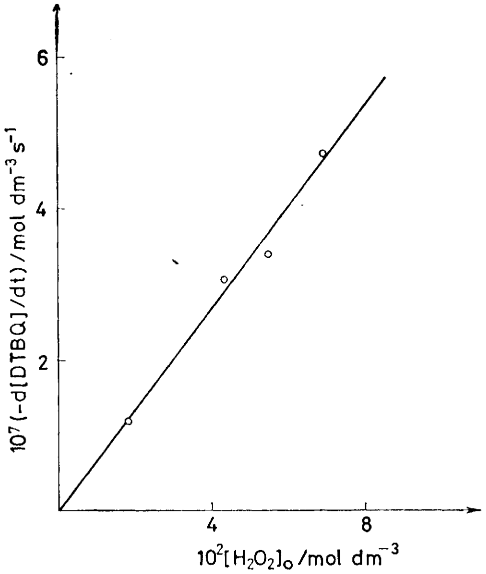


FIGURE 3 Initial reaction rates *versus* $[H_2O_2]$: [DTBQ] 1.94×10^{-3}M; *I* 0.1M; pH 9.08; 25 °C

Identical kinetic behaviour was found also at other pH values; however, the reaction rate varied significantly. At higher pH the reaction was found to proceed faster and at low hydroxide ion concentrations slower reaction rates were measured. By plotting the logarithm of $k_{obs.}$ against the pH a straight line was obtained in the pH range between 8 and 10 (Figure 4). The various pH values were adjusted by mixing 0.02M-Na_2HPO_4 and 0.02M-KH_2PO_4 solutions in 50% methanol (with an ionic strength of 0.1M-KNO_3) and the actual pH calculated according to equation (1). The $pK_{H_2PO_4^-}$ value for the 50% methanol solution was obtained from Born's

$$pH = pK_{H_2PO_4^-} - \log \frac{\gamma H_2PO_4^-}{\gamma HPO_4^{2-}} - \log \frac{[H_2PO_4^-]}{[HPO_4^{2-}]} \qquad (1)$$

equation as 8.97×10^{-9} dm^{-3} mol.[21] The calculated pH values were in good agreement with the data measured experimentally in 50% methanol.[22] This dependence of the reaction rate on pH is characteristic for base-catalysed reactions. In order to decide whether the reaction is subject to general or specific base catalysis, runs were made at constant pH and different buffer concentrations. The reaction rate showed no dependence on the HPO_4^{2-} and $H_2PO_4^-$ concentrations and then supports specific base catalysis.

In all these catalytic runs the ionic strength was adjusted with potassium nitrate to 0.1M; however, those with varying ionic strength showed linear plots of $\lg(k/k_0)$ against $I^{1/2}$ with a negative slope up to *I* 0.5M.

Based on the kinetic data rate equation (2) can be derived.

$$\text{rate} = k\,[DTBQ][O_2H^-] \qquad (2)$$

In basic media hydrogen peroxide is deprotonated in a fast pre-equilibrium to yield the anion O_2H^-, which as a nucleophile attacks the *o*-quinone in the rate-determining step.

The concentration of O_2H^- at different pH and H_2O_2 concentrations was calculated using K_{H_2O} 2.15×10^{-17} mol dm^{-3} and $K_{H_2O_2}$ 2.8×10^{-13} mol dm^{-3} at 25 °C (from Born's equation) according to equation (3). The rate

$$[O_2H^-] = \frac{K_{H_2O_2}}{K_{H_2O}[H_2O]}\,[H_2O_2][OH^-] \qquad (3)$$

equation (2) is then modified to (4).

$$\text{rate} = k\,\frac{K_{H_2O_2}}{K_{H_2O}[H_2O]}\,[DTBQ][H_2O_2][OH^-] \qquad (4)$$

From equation (4) and the general form [23] of specific base-catalysed reactions k_{obs} and k_{OH^-} can be calculated according to equation (5), since it is apparent from Figure 4 that $k_{OH^-} \gg k_0$ or k_{H^+}. The experimentally

$$k_{obs} = k\,\frac{K_{H_2O_2}}{K_{H_2O}[H_2O]}\,[OH^-] = k_{OH^-}\,[OH^-] \qquad (5)$$

obtained data for k_{obs}, those calculated for k_{OH^-} and k, and the activation parameters are collected in Table 1.

TABLE 1

Values of the activation parameters and of k_{obs}, k, and k_{OH^-} at various temperatures and [DTBQ] 1.62×10^{-3}M $[H_2O_2]$ 1.59×10^{-2}M, pH 9.08, *I* 0.1M

$t/°C$	19.5	20.2	25.0	30.1	36.2
$10^3\ k_{obs}/mol^{-1}\ dm^3\ s^{-1}$	3.66	4.21	7.90	11.6	21.50
$k/mol^{-1}\ dm^3\ s^{-1}$	10.5	12.1	22.0	33.5	61.5
$10^{-4}k_{OH^-}/mol^{-1}\ dm^3\ s^{-1}$	0.55	0.64	1.20	1.77	3.25

$\Delta H^\ddagger$ 76 ± 4 kJ mol^{-1}, $\Delta S^\ddagger$ 34 ± 1 J K^{-1} mol^{-1}

These kinetic observations are compatible with the mechanism in reactions (6) and (7). The deprotonated

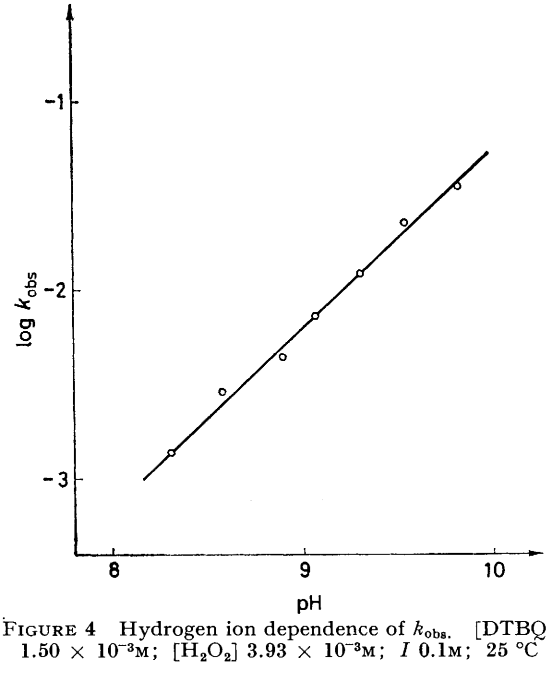
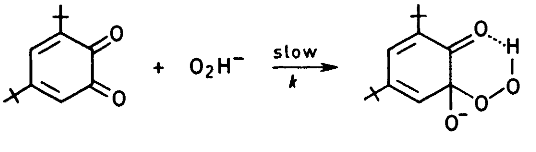


FIGURE 4 Hydrogen ion dependence of k_{obs}. [DTBQ] 1.50×10^{-3}M; $[H_2O_2]$ 3.93×10^{-3}M; *I* 0.1M; 25 °C

hydrogen peroxide attacks the carbonyl group at C(1) in a slow rate-determining nucleophilic reaction yielding the intermediate (2), which breaks down in a fast reaction presumably in two ways as suggested by the products formed.

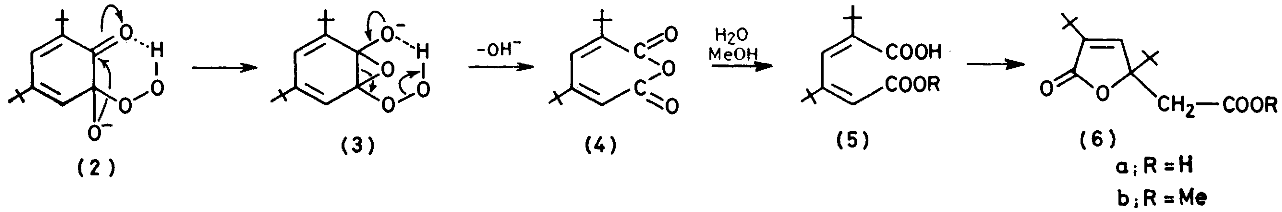
$$H_2O_2 \overset{K_{H_2O_2}}{\rightleftharpoons} H^+ + O_2H^- \qquad (6)$$



(7)

(1) (2)

The first route is outlined in Scheme 1 where DTBQ undergoes typical Baeyer–Villiger type reaction with hydrogen peroxide: intermediate (2) rearranges through (3) to 2,4-di-t-butylmuconic acid anhydride (4). The anhydride (4), whose amount was in the range 1—3% (g.l.c.) after the usual work-up, including acidification and the use of water–methanol (50 : 50) as solvent, was identified by m.s., *m*/*e* 236 (*M*⁺). It is solvolysed by the solvent mixture to the free 2,4-di-t-butylmuconic acid (5a) and its monomethyl ester (5b), which, however could not be identified in the products because they were lactonized, probably very rapidly, to 5-(carboxymethyl)-3,5-di-t-butylfuran-2-one (6a) and 5-(methoxycarbonylmethyl)-3,5-di-t-butylfuran-2-one (6b). The high solvolytic reactivity of 2,4-di-t-butylmuconic acid anhydride towards water and methanol [giving (6a) and (6b)] was demonstrated earlier.[16]



SCHEME 1

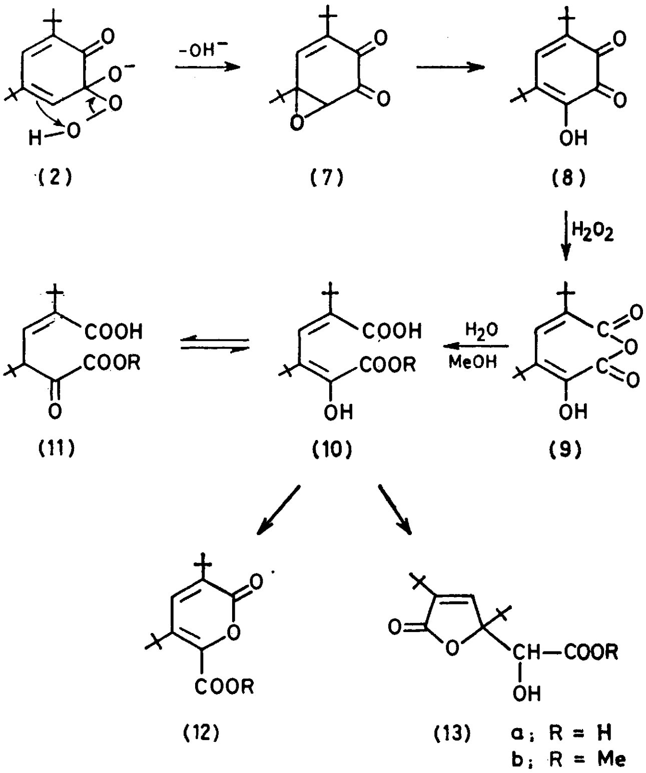
In addition a second mode of transformation of the hydroperoxide intermediate (2) can be assumed from the reaction products (Table 2) which is drawn in Scheme 2. According to this (2) is hydroxylated in an inter- or intra-molecular fashion, probably *via* the epoxide intermediate (7), at the C(6) position to give 6-hydroxy-3,5-di-t-butyl-*o*-benzoquinone (8). This then reacts with hydrogen peroxide present in excess in a similar reaction as in Scheme 1 yielding (9), the 5-hydroxy-derivative of (4). After solvolysis of (9), 5-hydroxy-2,3-di-t-butylmuconic acid (10) is formed, which equilibrates in a keto-enol tautomerism to (11) and is transformed through lactonization to (12) and (13). 5-Hydroxy-2,4-di-t-butylmuconic acid anhydride (9) could not be detected by g.l.c.–m.s. in the reaction mixture. We were also unsuccessful in finding 5-hydroxy-2,4-di-t-butylmuconic acid (10) in a similar manner. All other products, however, were found and their quantity determined as given in Table 2.

TABLE 2

Product composition of a typical reaction of DTBQ with H_2O_2 determined by g.l.c. after methylation with diazomethane

Compound	Yield (%)
(4)	1.6
(6b)	23.6
(11)	46.9
(12)	7.5
(13)	16.7

It is interesting to note that in this reaction there is probably no Michaelis-type addition of the hydroperoxide anion to the quinones. In this nucleophilic reaction (1) could also be converted into (8) through the epoxy-intermediate (7). This assumption is supported by the fact that neither the 3,4-epoxide nor the 4-hydroxy-derivative of 3,5-di-t-butyl-*o*-benzoquinone could be detected among the reaction products, which would also be expected as a result of a Michaelis addition of H_2O_2 attacking both the C(4) and C(6) positions of (1).



SCHEME 2

The reason for that may be that the bulky t-butyl groups n the C(3) and C(5) positions of (1) exert steric hindrance against an attack of the nucleophile O_2H^-. We therefore prefer the mechanism for this reaction outlined in Schemes 1 and 2, which is rather similar to the Weitz–Scheffer reaction.[24] An identical mechanism was proposed for the reaction of acrylonitrile with hydrogen peroxide with intramolecular epoxidation of the intermediate hydroperoxide to give the epoxide of acrylic acid amide.[25]

EXPERIMENTAL

Materials.—3,5-Di-t-butyl-*o*-benzoquinone [12] (1), *cis,-cis*-2,4-di-t-butylmuconic anhydride [16] (4), 5-(carboxymethyl)-3,5-di-t-butylfuran-2-one [16] (6a), 5-(methoxycarbonylmethyl)-3,5-di-t-butylfuran-2-one [16] (6b), 6-carboxy-2,4-di-t-butyl-2-pyrone [26] (12), and 5-(carboxyhydroxymethyl)-3,5-di-t-butylfuran-2-one [12] (13a) were prepared according to the literature.

Kinetic Measurements.—Reaction rates were followed by monitoring the disappearance of (1) at 414 nm using 5 mm cuvettes thermostatted at various temperatures in the cell housing of a Specord 75 IR (Carl Zeiss, Jena) spectrophotometer. The ionic strength was maintained at 0.1M by addition of KNO_3 and the pH was maintained between 8 and 10 by buffering with KH_2PO_4 and Na_2HPO_4. The reactions were carried out under pseudo-first-order conditions with the initial concentrations of (1) ranging from 10^{-5} to 10^{-3}M and the hydrogen peroxide concentration at *ca.* 10^{-2}M, which was determined by standard iodometric titrations. Rate constants were calculated from the standard equation over at least four half-lives using a least-squares best fit computer program. All kinetic measurements were run at least in duplicate using 50% methanol with fixed pH and ionic strength.

Product Composition.—In a separate experiment 3,5-di-t-butyl-*o*-benzoquinone (1) (2.20 g, 10 mmol), Na_2HPO_4 (1.64 g), KH_2PO_4 (0.53 g; pH 8.3), and 30% H_2O_2 (1 ml, 30 mmol) in 50% methanol (500 ml) were reacted under nitrogen for one week. The solution turned pale yellow. Two-thirds of the solvent was evaporated *in vacuo* and the pH adjusted to 5 with diluted HCl. It was extracted twice with ether (100 ml), dried ($MgSO_4$), and the ether pumped off *in vacuo* to give a pale yellow oil. This was treated with diazomethane and subjected to g.l.c.–m.s. analysis using a JEOL JMS-015G-2 instrument with an ionization potential of 75 eV and a 2.5 m 3% OV-1 on Chromosorb WHP, 100—120 mesh column with a temperature program of 6° min^{-1} from 125° and He as carrier gas. The following compounds were indentified and quantitatively determined on the basis of their mass spectra and compared with authentic samples: *cis,cis*-2,4-di-t-butylmuconic acid anhydride (4), R_F 13.5, *m/e* 236 (12%, M^+) and 221 (100); 5-oxo-2,4-di-t-butylhex-2-enedioic acid dimethyl ester, R_F 16.5, *m/e* 298 (3%, M^+), 242 (74), 239 (48), and 211 (100); 5-(methoxycarbonylmethyl)-3,5-di-t-butylfuran-2-one (6b), R_F 14.6, *m/e* 211 (100%), 197 (49), and 153 (28); 5-(carboxyhydroxymethyl)-3,5-di-t-butylfuran-2-one methyl ester, R_F 21.0, *m/e* 266 (69%, M^+), 251 (47), 238 (23), and 223 (100).

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